





# SAJOUS'S ANALYTIC CYCLOPEDIA OF PRACTICAL MEDICINE

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## PREFACE

**I**N THE preparation of this volume, two objects have been kept in mind: first, to make it a comprehensive yet clinical review of the advances that have occurred in medicine, surgery and the various specialties of the medical sciences in the last twelve months; second, to supply a useful and adequate ready reference volume for the general practitioner as well as the specialist. In this the editor and associate editors have been ably assisted by a group of contributors especially selected because of their interest and preëminence in the various subjects which they have reviewed.

This volume represents an earnest and conscientious effort to make readily available to the medical profession the important and outstanding advances that were made during the last year in the various fields of medicine and surgery.

Attention should be called to the fact that the format of this volume has been radically changed. The double column has given place to the single column page. Furthermore, where formerly all the subjects considered, regardless of the field of medicine or surgery to which they belonged were arranged alphabetically, in the present volume they have all been grouped under the main subject of which they are a part. For example, under the general head of medicine will be found sections devoted to allergy, cardiovascular diseases, gastrology, metabolism, nephritis, endocrinology, etc. Surgery is divided into abdominal thoracic and orthopedic surgery, likewise surgery of the genitourinary tract, cancer and the other subdivisions also properly fall under the general head of surgery. In addition to this, separate sections are given over to gynecology, obstetrics, pediatrics, neuropsychiatry, otolaryngology, ophthalmology, dermatology, radiology and other important subdivisions of medicine in its broadest sense. It is believed that this new arrangement will greatly add to the value of this volume as a work of ready reference, enabling the reader to find in a compact and condensed form the information which is desired on any given subject. Several new sections of timely interest have been added, notably those on hematology, rheumatism and rheumatoid disorders and physical therapy.

A liberal section has been devoted to General Therapeutics. Every effort has been made to emphasize treatment, all therapeutic suggestions having been clearly presented by the use of bold type and in addition to this, the question of treatment in its broadest sense has been given particular attention. Separate subdivisions have been devoted entirely to the consideration of such important subjects as dietetics and physical therapy.

In conclusion the Editor wishes to express to Dr. Edward L. Bortz in particular, as well as to the other members of the Editorial Board, his sincere thanks for the enthusiasm and cooperation which they have accorded him in the preparation of this work. He also wishes to express his appreciation of the valuable assistance rendered by Miss L. I. Weisgerber, in seeing this volume through the press and the preparation of the index. The publishers are to be congratulated on the excellent appearance of this volume and their liberality in the matter of illustrations.

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# MEDICINE

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# Allergy

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**ALLERGY.—DEFINITION.**—L. Martin (Ann. Int. Med. 8: 483 (Oct) 1934) reviews the definitions of 4 terms that are often ambiguously and erroneously used. They are *allergy*, *anaphylaxis*, *hypersensitivity* and *immunity*. He points out and directs attention to the fact that allergy and immunity can and should be dissociated. *Allergy* itself is a term often used to explain the unusual, but no word has been so maligned as immunization. Many procedures have been loosely explained by designating them as *immunity*. It is here used to set apart and describe the process of making an animal or individual capable of resisting the invasion of bacteria or the end-results of a bacterial toxin.

It is not necessary, as a great many have thought, to have an allergic reaction before immunity is brought into action. When a patient comes in contact with an offending protein, whether it be inhalation of pollen, the ingestion of food or the hypodermic injection of a specific substance, a reaction takes place. It is folly to call this response immunity. This individual is *hypersensitive*. In the hypersensitive state, there is a fundamental change in the animal's body functions.

The mechanism of immunity may be complex but that of *allergy* is not only intricate and involved but also mystifying and bewildering. An individual may be both immune and allergic, but the association is not essential. Allergic individuals who are immune may at any time become nonallergic and still remain immune. Animals which are allergic and immune may at any time be desensitized without losing their immunity and it is possible to immunize them without producing allergic reactions.

Allergy and immunity must be looked upon as separate reactions. The research in this field has been done almost entirely on animals. This may be a fertile field, the author believes, to work on human beings with the idea of immunizing them without making them hypersensitive. It is always well to remove allergy once it has been acquired and, if possible, to eliminate it, if possible, in the majority group of hereditary cases of allergic disease. By and large, allergy is hereditary but the offending atopy is a matter of chance.

**ALLERGIC SHOCK.**—Evidence that "*allergic shock*" is a clinical and pathologic entity in cases other than in those reactions to injections of pollens and sera is presented by G. L. Waldbott (Ann. Int. Med. 7: 1308 (Apr.) 1934). It is well known that the above phenomenon follows pollen and serum injections and is also observed during intradermal skin testing. The author also demonstrates that the same syndrome follows contact with certain foods or animal danders and that it is often found in cases of heat and cold sensitivity. This last is one of the most intriguing and extraordinary responses that the allergist is called upon to treat. It is termed "*physical allergy*."

*Anaphylaxis* is usually relegated to the realm of animal experimentation. Some believe the human anaphylactic shock is a definite entity and "*allergic shock*" has often been placed in the category of human anaphylaxis. Although the author refrains from using the terms anaphylactic and allergic shock almost synonymously, he believes that they are so closely associated that some day they will be viewed in the same light.

Ratner's work is the most convincing argument for the close association of these two all-important phenomena. So-called "*thymic death*," on which the author has done very exhaustive and important research, is also mentioned in connection with human anaphylaxis and "allergic shock."

Allergic shock is recognized as a clinical entity, while anaphylaxis in humans is not, and new light has probably been thrown on so-called "thymic death." These conditions, whether they are bound together in a common bond or are distant and separate reactions, are most important and should be highly regarded by the clinician.

Injection is usually thought to be the portal of entry in most cases of allergic shock but Waldbott completes the list from his own observations. His list of conditions, very few of which have any association with hypersensitiveness, are the following: Reactions due to thrombosis, fever, foci of infection, toxins, sera and, lastly, the definite reaction of a hypersensitive individual to a specific protein.

It is well to complete and confirm the clinical picture with a concise résumé of the pathological findings. The chief pathologic characteristic is edema, both locally and generally, especially in the skin and in the respiratory mucous membrane.

The foregoing two papers, although very scientific and possibly slightly academic, are very definitely of clinical and practical importance. Many times the clinician is confronted with obscure and unusual reactions. A better means of classification will aid materially in the recognition of significant shock phenomena.

**ASTHMA —Etiology.**—In a review of 337 cases, H. H. Moll (Brit. M. J. 2: 299 (Aug. 18) 1934) calls attention to the production of asthma reflexly, the most important source of this reaction being the nose and nasal mucous membrane. A reflex in any other part of the body may also act as a precipitating agent in the production of an asthmatic seizure. Distention of the stomach and rectum are the most notable examples. Reflex stimulation, according to some observers, may arise from some focal point in the lung itself.

The nasopulmonary reflex is notorious and is probably more of a factor than any of the other mechanisms. It has been shown that there is probably an asthmagenic or "trigger" area which, when stimulated, results in bronchospasm. This area has been described and bounded by the author. The complex nervous mechanism has also been demonstrated and traced physiologically and anatomically.

This reflex that has just been mentioned does not usually occur in normal individuals and it is believed that the nasopulmonary reflex must be unusually active. Most nervous arrangements and actions in an allergic person are exceedingly hyperactive. Back of these observations is the one underlying fundamental lack or overpreponderance of some factor that makes an individual hypersensitive or allergic.

Whatever the stimulus may be, it does occur and must be detected. It may be, and often is, a mechanical obstruction; a fundamental nasal abnormality or

a pathological polypoid growth may be present. In a great many instances, it is well to remove the source of irritation immediately, but there are many times when caution is the watchword in nasal procedures in asthmatics. Attacks of severe asthma have been precipitated by a simple nasal procedure, so it may be stressed that a complete allergic study must be done on all these cases.

Often the nasal symptoms do not disclose the part that is played by the nose as an etiological factor in asthma. Nasal abnormalities, both congenital and acquired, may be the end-result of an allergic condition. Some observers go so far as to state that the majority of nasal polyps are allergic. This is very dogmatic but has some element of truth in it.

Many cases of asthma are accompanied by nasal symptoms. In some cases the asthma has probably been precipitated by nasal abnormalities, but in others, the rhinological aspect is secondary to the patient's hypersensitivity or allergic condition. The intrinsic asthmatic with the focus of trouble in the nose differs widely from the extrinsic allergic individual with a generalized hypersensitivity to some extraneous protein substance. Caution and prudence are necessary in the contemplation and consummation of nasal procedures, both conservative and radical, in allergic patients.

**Prognosis.**—R. C. Grove and R. A. Cooke (J Allergy 5 621 (Sept) 1934) studied a group of 120 cases of asthma with infection with special emphasis on the rhinologic aspect. Intranasal sinus and radical antrum operations were performed on these patients. The follow-up of this group extended from 6 months to 3½ years.

The cases were divided into those who had an extrinsic sensitivity and those who gave no skin reactions. A division was also made between those who had had all nasal surgery completed and those in whom it had been incompletely done.

The results were as follows. In the group that had been completely operated, it was found that 82 per cent. were definitely improved; only 38 per cent. showed improvement in those that had not been completed surgically. In that group in which the patients were skin sensitive and completely operated, 88 per cent. improved and in those incompletely done of this type, 40 per cent. improved. The average for 120 cases was 70 per cent. If the cases are carefully selected and completely operated, the authors believe the results are decidedly hopeful.

L. N. Gay, in discussing this report, points out that great confusion exists as to the relative advantage of removing chronic infection in the sinuses or just providing adequate drainage. The many failures that have been encountered following both procedures have made Gay very pessimistic. With this, the reviewers decidedly agree.

Many reasons have been suggested for the large percentage of failures. They are as follows. Incomplete removal of all infected tissue; inexperience and timidity on the part of the allergist and rhinologist; the infection is of too long standing and the respiratory distress has extended over too long a period of time, most cases seen in the first year give better results.

The physician, according to Grove, should not be discouraged if results are not obtained immediately. There was a much higher incidence of complete relief

in the group after 1 to 2 years of observation. Nasal infection is a great source of anxiety and thought to the allergist.

**Treatment.**—The various **protein substances** that have been used over a period of time for nonspecific protein therapy, with varying degrees of success, are enumerated by T. S. Nelson and G. Duckworth (Lancet 2:650 (Sept. 22) 1934). Bacterial vaccines, tuberculin, broth, peptone, milk and sulphur have had their advocates. Autohemotherapy and autoserotherapy have been tried and also the urinary proteose of Oriel.

The *antigen-antibody response* is also explained in this review. The body seeks to protect itself against the invasion of any antigenic substance by the formation of antibodies. If these are circulating in the blood, the protein substance will be taken care of and neutralized; but if the antibodies are in combination with any cells, then a reaction will take place in this location. This reaction in man is known as atopy. The hypersensitivity is hereditary but the specificity is a matter of chance.

**Nonspecific protein therapy** is suggested to stimulate antibodies that will protect the cells in general, since it has been observed that when a specific response is elicited, often there is also a universal reaction in the body. It is believed that this is a response of the cells of the reticuloendothelial system.

**Colloidal sulphur** was used in this series of cases along with the other substances mentioned.

Van Leeuwen was the first to use a suspension of sulphur in olive oil. It has often been held that the results obtained from the use of this substance were in the production of hyperpyrexia. On this account, the authors abstained from using fever-producing doses as far as possible. The doses given varied from 0.5 c.c. of a 1:10,000 dilution to 1 c.c. of a 1:1000 dilution.

All degrees of asthmatics, from mild to severe, were treated in this group. Complete studies from the standpoint of sensitivity, medical care and operative routines were done.

In the cases treated by **autogenous vaccine**, it has been previously observed and here confirmed that the patients with marked upper respiratory infection are particularly resistant to treatment. This is especially true of those that have streptococcal infection. Most of the vaccines were made from sputa obtained as much as possible from the bronchi.

The following conclusions have been reached. First, protein injections are markedly beneficial in *asthmatics*, secondly, colloidal sulphur produces good results and its use is thereby justified, but the best results were obtained by the use of a broth designated by the above authors as broth "B B W". A short prophylaxis at least is produced, as there must be an awakening of the antibody-forming tissues so that there is an overproduction of circulating antibodies, a stimulus producing a general as well as a particular response. All in all, it has been concluded here that the outlook for an absolute cure in atopy is rather gloomy at the present time.

B. Z. Rappaport, C. I. Reed, M. L. Hathaway and H. C. Struck (J. Allergy 5:541 (Sept. 1934)) published an account of 6 cases of *hay fever* and *asthma*

treated with **viosterol** of high potency. Their results were sufficiently encouraging, so that more investigation has been undertaken. The procedure, results and conclusions are herewith presented. The statistics in this paper are tabulated on 212 cases.

Of the whole group, 68 subjects received only viosterol; another group, 69 in number, received both pollen injections and viosterol therapy. This latter group had not received pollen injections the previous year. Another group on which observations were made included those patients who received viosterol and pollen injections and who had also received the pollen injections the year before. In this last, a comparison could be drawn between the results of pollen therapy alone the year before and the results of pollen therapy with viosterol.

It is very difficult to evaluate the results obtained, as the personal impression of the degree of relief is variable with each individual. In order to make this as accurate as possible, the patients were requested to make a daily observation of the severity and the number of attacks of sneezing, the presence or absence of nasal and eye symptoms and asthma, the number of hours of sleep during the night, and the estimation of the individual himself as to the severity of any of these symptoms. As far as possible, the results were compiled by one person receiving the data from the same subject at each visit.

The classification for the evaluation of results included the amount of relief, from complete to slight or no relief. A numerical index system was tried, using 10 to equal complete relief and 0 meaning no results.

The initial dosage of viosterol known as 10,000X was given daily. This was started 2 to 4 weeks before the symptoms were usually experienced by the patient. A control group of 30 patients was given corn oil, as viosterol is dissolved in corn oil.

The rôle of plasma calcium and calcium metabolism must be considered in this work, as an increase in calcium is reputed empirically to give beneficial results in allergic individuals. The blood calcium was directly proportionate to the amount of viosterol given in most cases, but the plasma calcium reading had no relation at all to the degree of relief of symptoms.

It is concluded by the authors of this work that the results obtained were not due in any way to an increase in the concentration of blood calcium. The only consistent and significant factor in blood chemistry was in the potassium-calcium ratio. The general level was lowered. Further study on this subject is in progress.

In the group of 212 patients with *seasonal hay fever and asthma*, it was found that the combination of **pollen injections** and the administration of **viosterol** of high potency is more efficacious than either used alone. The action of the viosterol has not yet been determined, but it is not linked or allied to the calcium mobilizing power of the viosterol.

The dose of the 10,000X viosterol was 2 to 10 drops daily, depending upon the susceptibility of the patient and not upon the severity of his symptoms or clinical signs.

This new therapy for seasonal hay fever and asthma strikes a note of rationality and affords, it is believed, an important adjunct to the armamentarium for the treatment of allergic disease

**HAY FEVER.**—*Treatment.*—M. R. Lichtenstein (J. Allergy 5:230 (Mar.) 1934) has studied very thoroughly the efficacy and practicability of the treatment of hay fever by the **intravenous injection of pollen extract**. He believes that at present it is to be considered an experiment, to be used only by those who have had wide experience in allergy

In the small group of patients, the pollen dosage varied from 10 to 2000 units given from once to twice weekly. One patient received only 1 injection and 15 injections was the highest number given 1 individual. This can be compared with the 28 to 33 injections given subcutaneously to 4 control patients. The usual number of treatments given in most clinics by the latter method varies from 25 to 40.

Many different types of *reactions* were noted and only in one was there any sign of a collapse reaction. This was believed to be an overdose for the type of patient in which it was used. Erythema, locally, and urticaria, generally, were observed. Hay fever-like manifestations in the nose also followed in several instances. A mild sense of constriction simulating an asthmatic seizure appeared twice in one patient. These untoward symptoms were relieved by **adrenalin**.

There was a marked diminution in the skin reactivity following intravenous therapy. This was also observed in one of the control cases and a slight decrease in the other controls.

The author has indicated previously that he was endeavoring to ascertain the practicability of the intravenous method. To be useful, it must also be safe and effective. It seems that the safety of this method is the most important point in question and it can be settled only after sufficient trial. Scientifically, this method should be the best method of administration because in subcutaneous treatment there is always the danger of overdose, due to rapidity of absorption and accidental intravenous injection. The hypodermic method has the advantage of the tourniquet, but the intravenous has unlimited possibilities of dilution and slow rate of injection. Any mistake in dose in the intravenous method would be very dangerous.

The safety, usefulness and practicability of the intravenous method of pollen administration can only be determined after a long series of cases has been treated. It is a method to be used with extreme care and under close supervision.

L. Unger and M. B. Moore (*Ibid* 5:561 (Sept.) 1934) report the results of their treatment of a series of cases with a 5 per cent **dextrose solution**. Extracts of pollen made with saline solution or saline and alcohol are notoriously unstable. Saline and glycerin solutions are much more stable and excellent results have been reported from the use of the latter.

The glycerin extracts are very painful on administration and also unsuitable for intradermal testing. It is most difficult also to force these solutions through very fine needles. The 5 per cent dextrose is almost as stable as the glycerin products.



With the above in mind, these observers treated 113 patients with the dextrose solution mentioned and the results were compared with pollen therapy in the same group with glycerio-saline extracts. The relief obtained was practically the same in both procedures and constitutional reactions occurred in about the same number of individuals.

After a number of skin tests, it was found that the dextrose extracts deteriorated very little, if any, more than the glycerin solutions. Both types retain their diagnostic and therapeutic potency for a period of probably 30 months. The slight reduction in strength can easily be controlled by close observation. Also, these two types of solutions remain stable even after long refrigeration and incubation.

The retention of a uniform potency in pollen extracts assumes a rôle of major importance, especially in perennial treatment, and as both the glycerin and dextrose solutions retain their strength to a certain degree, they are indicated especially in the year-round treatment. As the dextrose extract is much less painful, easier to handle and better testing material, the authors believe it is the best extracting and diluting fluid yet devised in treatment by the pollen method.

G T Brown (*Ibid.* 6:86 (Nov) 1934) presents his experiences in the treatment of hay fever in general and in maximum dosage **pollen therapy** specifically. His discussion, the reviewers believe, is of great interest both to the practitioner doing allergy and to the allergist. Methods vary considerably, procedures are numerous, and the type of extract used is often a matter of individual preference, each type giving practically the same percentage of successfully treated cases.

This observer favors at present a **glycero-saline extract** containing 46 per cent. glycerin and 6 per cent. sodium chloride. It is believed that this type of extract has a higher potency, and a nitrogen content has been demonstrated. This fluid does not give local irritation to any appreciable degree and an objection is here raised to the dextrose solution mentioned in another section. His opposition to this extract is based on the feeling that any dextrose fluid is a fertile field for the growth of any bacteria or fungi unless controlled by a relatively strong antiseptic. Glycerin and saline extracts in the dilutions mentioned above are highly recommended.

Cutaneous tests are better done with a certain percentage extract than with dry pollen dissolved by sodium hydroxide. As this is the case, it is most advisable to treat patients with whole pollen extracts.

Cases of any season should be treated with all of the causative pollens. Many patients have both a grass and weed sensitivity. There are various ways of attacking this problem as the season of activity in the spring coincides with the preseasonal therapy for fall cases. Brown attacks this problem by continuing the maximum dose received in the early treatment through the grass season while completing the graduated scale of ragweed therapy. If the maximum dose of grass is received before the fall preseasonal injections are started, then at the onset of ragweed therapy the spring treatment is stopped. It may be well to

continue the grass therapy at intervals, whether or not the maximum dose is reached, it is believed

Care must always be exercised during any period of activity because of pollen absorption from the air which may or may not be a factor, depending on the time, weather conditions, and symptoms.

The following table by Brown should be of interest and perhaps of aid in approximating the amount of pollen given in general. It is very clear and instructive.

AA or 1	100,000 equals	10 pollen units or	0.01 mg. of pollen per c.c.
A or 1	10,000 equals	100 pollen units or	0.1 mg. of pollen per c.c.
B or 1	1,000 equals	1,000 pollen units or	1.0 mg. of pollen per c.c.
C or 1	100 equals	10,000 pollen units or	10.0 mg. of pollen per c.c.
D or 1	10 equals	100,000 pollen units or	100.0 mg. of pollen per c.c.

He begins treatment with an initial dose of 0.05 c.c. of a 1:10,000 dilution which he has designated as A strength. An occasional very highly sensitive patient may require very much smaller doses at the beginning and, at times, 0.1 c.c. of 1:100,000 has been the first dose. This, according to the above table, is 1 protein unit.

It may be well at times to test each patient with serial dilutions and begin treatment with 0.1 c.c. of the strongest dilution which does not react. Children are usually given the same dose as adults.

Injections are given *subcutaneously* rather than into the skin, or intradermally. Intradermal therapy is painful and cosmetically inadvisable. In giving subcutaneous injections there is much less likelihood of introducing an amount of the extract into a vein and often a local reaction may be an index to the degree of increase in subsequent injections. This is much less noticeable if the injection is given intramuscularly.

This author believes that the results obtained in the treatment of seasonal hay fever are directly proportionate to the size of the dose reached preseasonally. He uses maximum dosage pollen therapy as much as possible and the doses given are quite large. He gives as high as 100,000 to 200,000 pollen units or 1 to 2 c.c. of a 10 per cent extract. This is, indeed, a large dose, but the best results are obtained if large doses are reached. Treatment is stopped in those patients who have attained this dosage as soon as active pollination begins. If the maximum dose is not reached, the dose attained preseasonally is continued through the pollinating period at weekly intervals. If any untoward reaction occurs, the succeeding dose is slightly decreased.

If symptoms develop during the season in those who have obtained the maximum dose preseasonally, then small doses of 5,000 to 10,000 pollen units are given at intervals. It is the goal in some cases to eradicate the skin sensitivity, and the more completely this is accomplished the more permanent are the results. Experience has shown that skin desensitization is a very confusing and disturbing sign and may or may not occur whether or not the patient has obtained relief. It is felt that if the reactivity has been eradicated from the skin, it is highly probable that desensitization of the mucous membrane has been accomplished.

The amount of symptomatic relief and also the degree of skin desensitization may probably be directly dependent on the dosage given. Large doses of pollen extract may be given with safety if meticulous care is exercised in regulating the preliminary doses and succeeding increases in each patient individually.

**INSULIN ALLERGY.\***—A very complete review of the literature on insulin allergy is given by M. T. Davidson (*J. Allergy* 6:71 (Nov.) 1934) and a case of hypersensitivity is reported.

Early in the treatment of diabetes with insulin, many *reactions* occurred. Most of those reported were local, but there was a small percentage of constitutional reactions. Most of the untoward effects were produced by the extraneous protein which carried the insulin, *i. e.*, beef, pork or other animals.

The manufacture of insulin has been greatly improved. The end-product is highly refined and most of the extraneous material has been removed. It has been shown in a number of cases that the offending protein is crystalline insulin which is very probably not the same protein as human insulin.

Tuft reported 2 cases in 1928, one due to extraneous protein and the other due to insulin itself. Allan and Scherer reported 100 cases in 1932, 84 of which were mild local reactions, 12 severe local reactions, and 4 constitutional reactions. The local as well as the systemic reactions were of varying degrees. The constitutional manifestations may be urticaria, angioneurotic edema, asthma or any of the other allergic responses.

Many other cases of varying severity have been reported from time to time. The incidence of constitutional reaction is comparatively rare and a great many of the local reactions have been reported as clearing up spontaneously.

The most usual constitutional manifestation is *urticaria*. In a case reported by this author, it was found that the patient was sensitive not only to beef and pork insulin, but also to crystalline insulin. Very marked and severe urticaria was the rule after injection of insulin. This symptom was usually relieved by **adrenalin** and **ephedrine**. If the diabetic condition had persisted, desensitization was contemplated by the method of Besredka and Gloyne for use in horse serum sensitivity cases. An attempt at passive transfer gave negative results.

J. A. Murphy, J. T. Beardwood and M. M. Miller (*Ibid* 5:606 (Sept) 1934) report 2 cases of *insulin hypersensitivity* manifesting itself by generalized reaction, one as *urticaria* and the other as an *asthmatic* seizure. The one patient was definitely allergic and the other was not. The percentage of local reactions is believed to be relatively higher, but only 2 cases of generalized reaction due to insulin hypersensitivity were found in 940 cases using insulin in the treatment of diabetes.

The first case presented reacted to all types of commercial insulin for which she was tested. Her major reaction was to crystalline insulin. Fortunately, this patient's condition was readily controlled by diet, so that it was not deemed necessary to desensitize her to relieve the symptoms and signs. This patient had no previous personal history of allergy and no hereditary history of allergy in the family.

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\*See also Section on METABOLISM.

An attempt at passive transfer was done both in a diabetic and a normal individual. Both attempts were not sufficiently positive to make them believe that the transfer had been successful.

In the second case, it was discovered that the patient had previously suffered with fairly severe bronchial asthma. Her insulin hypersensitivity manifested itself as an attack of asthma. The insulin used had been obtained from pork.

This patient was skin tested on 2 occasions about a month apart and she reacted to all types of insulin by the intradermal tests. She also reacted to pork protein, but not to beef protein. After being placed on beef insulin, she had no untoward reactions.

Both cases reported had reactions from injections of insulin. The one developed urticaria, the other asthma. One case was a known allergic and the other was not. Both had had previous insulin injections. A change of the source of insulin helped one but not the other.

**SOY BEAN ALLERGY.**—W. W. Duke (J. Allergy 5: 300 (Mar.) 1934) presents a case demonstrating quite clearly a soy bean sensitivity. This substance is so universally used in many preparations that it may be a factor in a great many cases of allergy. It may be found in confections, breads, canned foods and pastry. It is quite often used in substitution foods and supplementary diets. Soy bean oil may be found in paints, soap, ink and lubricating materials.

The case reported in this summary was a man who lived near and was employed in a soy bean mill. He had severe reactions upon drinking milk from cows fed on soy bean fodder. He was highly reactive to all preparations of this product.

The scratch test for soy bean was markedly positive. Reactions were also noted to several grasses and low and high ragweed. If the soy bean oil was filtered through stone, it gave no reaction. Passive transfer was demonstrated very easily.

Soy bean was found to be quite indestructible as it stood autoclaving for  $1\frac{1}{2}$  hour and boiling for 2 hours with dilute hydrochloric acid and sodium hydroxide without being rendered inert. On testing individuals working in a soy bean mill, a small group was found positive. There is a strong possibility of sensitization in those individuals who have a close contact with preparations containing soy bean.

**SENSITIZATION TO SODIUM MORRHUATE.**—Four cases of sensitization to sodium morrhuate with resultant allergic-like reactions to its use as a sclerosing substance for varicose veins are reported by L. M. Zimmerman (J. A. M. A. 102: 1216 (Apr. 14) 1934). One very severe anaphylactoid reaction appeared and a milder attack presented itself in another patient. The other 2 cases manifested only urticaria. No hereditary history of allergy was noted in the 2 cases of generalized symptoms.

Intradermal tests for this preparation were positive in all cases. Scratch tests in a group observed by Geza de Takats were uniformly negative. This has been the case in a group of 30 allergic individuals tested for this substance by the reviewers of this section.

Several minor reactions were noted in a few highly allergic individuals. Intradermal reactions have been reported in several controls, so it is possible that this preparation may produce a nonspecific irritation.

The source of these untoward symptoms has not definitely been designated. Sodium morrhuate is a solution of saponified cod-liver oil. Whether there is a definite allergic reaction or a complex biochemical phenomenon is a question. Also, it may be possible that the introduction of this substance into a vein produces hemolysis and liberation of protein substances that produce the reaction.

It has been found that sodium morrhuate is the most widely accepted agent for sclerosing varicose veins. Two cases presented very severe shock-like reactions. The author believes it is well to test all patients by the intracutaneous method, especially in those who have had a rest period of several weeks after the previous injections. If there is any positive reaction following actual injection of the material, another sclerosing agent should be selected for subsequent therapy.

**SENSITIZATION TO POISON IVY.**—H. W. Straus (J. Allergy 5: 568 (Sept.) 1934) follows up his report previously given on the sensitization of *newborn infants* to poison ivy. The first group was sensitized by ingestion of and skin application of an extract. Another group was exposed by means of a patch test only. The sensitization which was generalized over the entire skin was positive in 72.9 per cent. of a group of 48 children.

This presentation deals with a group that was sensitized by ingestion and subcutaneous injection of a solution of poison ivy extract. A 10 per cent. alcoholic extract was used and it was administered by placing 2 drops on the back of the tongue. Each infant was given about 10 drops. When a patch test was done 1 week later, all tests were negative. This was done in 10 infants.

Ten other children were given a subcutaneous injection of 1 c.c. of a 10 per cent. solution of an alcoholic extract. Nine children gave a negative patch test 1 week later. It is highly possible that the one positive test may have had some epidermal contact with the extract, although every precaution was taken. An accidental test for potency was demonstrated when a nurse developed the typical poison ivy lesions after spilling some of the material on her hands.

It is concluded from these results that the best, if not the only, way to sensitize an individual to poison ivy is by direct contact with the epidermis.

Six of these patients were tested by the patch method for both poison ivy and sumac. Four of the cases had strongly positive reactions to both. One was suspicious for both and the last one was negative to the two types of poison.

From this latter observation, the author feels that the active principal in ivy and sumac are immunologically the same. Therefore it seems that in the treatment of these conditions by the injection method, the extract of either one can be used in the treatment of one or both conditions.

The percentage of persons susceptible to *poison ivy* and *poison oak* has been investigated by W. C. Spain, J. M. Newell and M. G. Meeker (*Ibid.* 5: 571 (Sept.) 1934). The work was done on adults only. These individuals were tested with an alcoholic extract of the dried leaf powder. The patch test was

used and different dilutions applied. The technic is given in detail and the results adjusted to the basis of 100 patients as being regularly observed.

It was concluded that, under equal conditions of exposure, the percentage of human beings susceptible to poison ivy and poison oak varies similarly to the actions of drugs and other physiologic stimuli in general according to the law of Weber-Lechner. Mathematically, it has been demonstrated in this paper that the percentage varies as the logarithm of the concentration of the substance.

**SURGERY AND ALLERGY.**—Rose André and R. C. Grove (J. Allergy 5: 536 (July) 1934) report a survey of a group of 204 allergic patients who had *nose and throat surgery under general anesthesia*. Their findings are most important, as the allergist and rhinolaryngologist are confronted with 2 problems: (1) When to operate on an allergic patient, and (2) what type of anesthesia to use.

It has been found from the observation of this series that general anesthesia is safe in allergic patients. It may even be used in the severe asthmatic if the case is carefully selected and prepared. A method which employs small amounts of anesthesia with **carbon dioxide** and **oxygen hyperventilation** is found to be the one of choice. In this group, pulmonary complications were noticeably absent.

Harry Schenck, in discussing this paper, states that, from the conclusions in this study, it would seem that general anesthesia is as safe in allergic patients as in others. He cautions that the anesthetic and operation should not be entrusted to average operators and anesthetists. It is most necessary that all patients be subjected to painstaking preoperative treatment and the proper attention must be given to basal anesthesia and hyperventilation at the close of the operation. **Avertin** has been used successfully by the above authors and has been found satisfactory by others.

Many operations on the *upper respiratory tract* in allergic patients can and should be done under **local anesthesia**. This again calls for selectivity of cases as to temperament and physical condition. Schenck advises the use of local anesthesia in the radical operations of the Caldwell-Luc and the Ferris Smith types. This is suggested because it minimizes shock and gives the operator a dry field of operation.

A great deal may be said for both types of anesthesia, but the importance of the correct selection of cases for each form must again be emphasized. Whether the operation is done under local or general anesthesia, the preoperative care and postoperative management assume rôles of extreme importance.

# Arthritis and Rheumatoid Conditions

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**ARTHRITIS AND RHEUMATOID CONDITIONS.**—*Introduction.*—A partial measure of the rate at which the literature bearing upon diseases of joints, muscles and tendons is increasing may be indicated by the fact that upwards of 600 new titles are included in the annual supplement to the library of the *Ligue Internationale Contre le Rhumatisme*, covering the period from May, 1933, to June, 1934. These titles, representing books, papers and reports upon various phases of rheumatism, constitute but a fraction of all the items appearing in the widely scattered medical journals which carry articles upon related topics. The evident desirability of making the advances in this broad field more readily available has led to the organization of several national and international congresses, and the establishment of journals devoted exclusively to the consideration of these diseases. As representative of these converging channels through which the contributions to the literature of rheumatism are beginning to flow, the following may be mentioned: *Quatrième Congrès International contre le Rhumatisme*, held at Moscow, in May, 1934, the proceedings of which appear in *Acta Rheumatologica*, *Conference Scientifique Internationale du Rhumatisme Progressif Généralisé*, at Aix les Bains, in July, 1934, the American Association for the Study and Control of Rheumatic Diseases, at Cleveland, Ohio, in June, 1934, the proceedings of which appear in brief in the *Journal of the American Medical Association*. 103·1732 (Dec 1) 1934).

In addition to the proceedings of these conferences, reference should be made to other relatively condensed sources of new data bearing upon the problem. A new monthly journal, "Revue de Rhumatisme," was inaugurated in France, in January, 1934. The "Acta Rheumatologica," a bi-monthly journal, continues as the official organ of the *Ligue Internationale Contre le Rhumatisme*. "Rhuma-Jahrbuch" serves as a review of the German literature. The American Committee for the Control of Rheumatism, has supplemented its activities in the field of making new advances more readily available to the profession by fostering under its auspices the preparation of a comprehensive critical digest by P. S. Hench, W. Bauer, A. A. Fletcher, D. Christ, F. Hall and P. White, under the title of "The Present Status of the Problem of Rheumatism. A Review of Recent American and English Literature on Rheumatism and Arthritis," which is to appear in the *Annals of Internal Medicine*.

These facts serve to illustrate not only the widespread active interest in the topic, with some of the comprehensive reviews available, but also the utter futility of any attempt to present here even so much as a complete bibliography and much less an abstract of the voluminous literature.

**Incidence.**—It has been noted by R. Pemberton and R. B. Osgood ("The Medical and Orthopaedic Management of Chronic Arthritis," MacMillan Co., New York, 1934) that the disease is more common in the temperate than in the tropic and arctic zones, although both atrophic and, particularly, hypertrophic arthritis do occur and apparently have existed in all climates and at all times. While it is recognized that environmental and social conditions may exert an influence upon the incidence of the disease, it does not appear to these authors

that either atrophic or hypertrophic arthritis is peculiar to the poor or to the rich. Insofar as the effects of occupational and environmental factors may be related to types, it appears that exposure to cold and damp predisposes to the production of atrophic arthritis, while the subjection to joint injury and strain is more important in the production of hypertrophic arthritis. These authors reaffirm the general impression that atrophic arthritis is somewhat more common in women than in men, whereas hypertrophic arthritis is encountered in the same frequency among both sexes. Atrophic arthritis occurs from early to mid-life, whereas hypertrophic arthritis rarely appears before the age of forty. Atrophic arthritis is more commonly seen in persons of the slender type, while hypertrophic arthritis is more often observed in persons of the stocky type.

It may be observed in this connection that R. Pemberton and T. F. Bach (unpublished data) have noted that a significant degree of anemia is present in hypertrophic as well as in atrophic cases. In this same series, evidence of a direct or collateral occurrence of the disease in the family was noted in over 50 per cent of both atrophic and hypertrophic cases. In two-thirds of both types evidence of gastrointestinal dysfunction was observed. Likewise, focal infection was found in the same relative frequency in each type.

There are, of course, exceptions to these generalizations. In general practice P. S. Hench (Demonstration, A. M. A. Scientific Exhibit, Cleveland, 1934) has estimated that of 100 patients visiting the physician for rheumatic complaints, there are approximately 25 to 30 with hypertrophic arthritis, 35 to 40 with atrophic arthritis, 10 to 15 with fibrositis, 7 to 10 with traumatic arthritis, 3 to 5 with gouty arthritis, 2 with gonorrheal arthritis, and 3 to 5 with miscellaneous types including tubercular and tabetic arthritis. The relative frequency with which these cases occur may vary in different geographical locations, but the general preponderance of chronic arthritis of the two types probably holds for most places.

Data bearing upon the general incidence and social cost of rheumatoid disease are cited by L. I. Dublin ("Chronic Arthritis and Rheumatoid Affections," Chapt. I, by B. L. Wyatt, Wm. Wood and Co., New York, 1930) from data taken from large surveys conducted by insurance companies in several parts of the United States. The general attack rate is about 16.5 per 100,000 and constitutes about 8.5 per cent of all illness. In some large cities the number of persons affected was found to be second only to the number of persons injured by accident. During 1928, one company paid 8.5 claims for rheumatoid disability for each 1000 males insured. In England, the National Health Insurance Scheme paid 10 per cent of 75,000 claims for rheumatoid disability. The same writer cites data indicating that the incidence of rheumatoid disease is higher among persons subjected to exposure, including quarry workers, iron miners, steam railroad, subway and elevated employees, workers in paper pulp wood, steel, iron and lead plants, than among inside workers.

P. B. Matz (New England J. Med. 209:597 (Sept. 21) 1933) reports that during 1931, 35,000 ex-service men received \$10,000,000 in disability compensation caused by arthritis. This sum represents 4.7 per cent of all veterans' benefits and 6.4 per cent of the beneficiaries of the Veterans Administration.

**Etiology.**—Many factors contribute to the production and condition the course of chronic arthritis and by virtue of this must be evaluated in any consideration of etiology. Newer work has served to reemphasize this situation. Among such factors, the relative importance of which appear to vary in different individuals, are included heredity, constitution, body build, sex, age, trauma, infection, parasitism, allergy, fatigue, exposure to cold and damp, endocrine dyscrasias, nutrition, disturbances of intestinal, circulatory, respiratory and nervous systems.

Many recent contributions bear upon the rôle and nature of the influence of *bacteria*

In 251 cases (H. A. Nissen · New England J. Med. 210:92 (Jan 11) 1934), 123 of which were under 40 years of age, 38 per cent. showed definite or marked sclerosis. Foci were present in varying but not marked percentage. A. Steindler (J. A. M. A. 103:1732 (Dec. 1) 1934) has reported the incidence of foci of infection in 17 per cent. of 520 cases of atrophic arthritis and in 17.7 per cent. of 240 cases of hypertrophic arthritis.

S. S. Lichtman and L. Gross (Arch. Int. Med. 49:1078 (June) 1932), in a study of 5233 blood cultures, found positive evidence of streptococci in 4 per cent. of both rheumatic and nonrheumatic groups.

While the way must be left open to the view that infection may play a significant rôle in the etiology of hypertrophic arthritis, the evidence indicating that arthritis may have an infectious etiology is largely adduced from cases of atrophic arthritis.

In addition to those instances in which more or less direct evidence indicates an etiological relationship of bacteria and active arthritis, several somewhat indirect lines of evidence have been advanced. The fact that the early and most prominent pathological change characterizing atrophic arthritis is proliferation and the usual clinical picture shows inflammation, are cited as evidence of an *infectious* etiology. M. H. Dawson (J. Exper. Med. 57:845 (May) 1933) suggests that the similarity of subcutaneous nodules in atrophic arthritis and rheumatic fever indicates a similar etiology.

The presence of round cell infiltration noted by N. Allison and R. K. Ghormley ("Diagnosis of Joint Disease: A Clinical Pathological Study of Arthritis," Wm. Wood and Co., New York, 1931) to be present in both types, but particularly in the atrophic, is likewise cited as evidence of an infectious or toxic origin.

The concept of metastatic infection of joints from foci of infection does not receive unanimous support from all workers, many of whom have failed to obtain positive cultures from the joints and from the blood. E. C. Rosenow (Arch. Int. Med. 51:327 (Mar.) 1933) has, however, further developed the conception of elective localizing power of bacteria in arthritis, having found that bacteria isolated from areas of infection in arthritics possess a characteristic cataphoretic velocity or rate of migration in an electric field. This author further reports data indicating that the blood serum from arthritics possesses the property

of slowing the cataphoretic velocity of streptococci isolated from cases of arthritis

The possibility that organisms may be transient invaders of joints from foci or from the gastrointestinal tract and there act as temporary irritants, has been advanced by R. Pemberton, E. G. Peirce and T. F. Bach (M. J. and Rec 138 445 (Dec. 20) 1933) on the basis of experimental studies and clinical experience with diet on the changes in the alimentary tract. Such a mechanism might provide for the direct action of bacteria and at the same time account for the irregular occurrence of positive cultures.

Regardless of the hypothetical means by which bacteria may exert an etiological influence, it appears that they do so by virtue of the substances which they produce or which they contain. It is further evident that the pathological changes induced in chronic arthritis are not like those seen in frankly septic and purulent joints. It, therefore, appears probable that the lesions are induced through the intermediation of physiological processes actuated at a distance. This concept has been restated by A. F. Coburn (Am. J. Dis. Child 45 933 (May) 1933), who describes the sequence of events in rheumatic fever somewhat as follows: A patient in the "rheumatic state" following the development of a streptococcus infection in the upper respiratory tract experiences an asymptomatic phase, during which period there is an increase in antibodies to the extent that there is an increase of immune bodies in the peripheral circulation. Coincident with this phase the rheumatic state becomes activated.

There is evidence that something of similar nature plays a part in chronic arthritis. Antibodies which agglutinate strains of bacteria and precipitins which precipitate chemical fractions of such organisms are found in the sera of atrophic arthritides. Such substances are considered by M. Heidelberger (Medicine 12 279 (Sept.) 1933) to be chemical variants of plasma proteins produced at the site of serum protein formation under the influence of foreign substances. Even in the absence of finding viable organisms, the presence of antibodies toward them is properly considered as evidence of the fact that the bacteria have been present. E. F. Nicholls and W. J. Stansby (J. Clin. Investigation 12 505 (May) 1933) found a high agglutinin titer in many atrophic arthritic sera against a "typical strain" AB13 and note the absence of this reaction in most hypertrophic sera.

M. H. Dawson, M. Olmstead and E. L. Jost (J. Immunol. 27 355 (Oct.) 1934) confirm the contrast between atrophic and hypertrophic cases, but consider that this reaction is group, rather than strain, specific with *Streptococcus hemolyticus*. The reaction, according to the latter workers, is furthermore a true immunological one and not due to a nonspecific chemical property of the serum, as might have been considered on the basis of data by W. S. Tillett (Bull. Johns Hopkins Hosp. 50 270 (Apr.) 1932), indicating that the agglutination reactions of sera with streptococci are often due to the high level of fibrinogen which characterizes the response of the body to infections of many different sorts. In a series of cases of atrophic arthritis the sera reacted with *Streptococcus hemolyticus* and with group specific fractions of the organism in high dilution, whereas in 79 control cases, positive reactions were not found in significantly high dilution. The reactions cited do not exactly parallel the clinical activity

of the arthritic process. Further investigation is necessary to determine whether the frequent circumstantial evidence of the presence of hemolytic streptococci is of primary or of secondary importance in regard to etiology. In spite of the necessary limits of interpretation, these facts do reflect part of the dynamic pathology of the disease insofar as they provide evidence of a deviation from the usual course of physiological processes which must be evaluated in any serious attempt to understand the nature of the origin of disease.

In the same category, mention should be made of the presence in atrophic arthritis of an increased sedimentation rate and of a "shift to the left" of the polymorphonuclear cells.

W. K. Myers, C. S. Keefer and T. W. Oppel (J. Clin. Investigation 12: 279 (Mar.) 1933) have noted that there is relatively high incidence of sensitivity to nucleoprotein of streptococci among atrophic arthritics, but this sensitivity does not strictly parallel the disease. C. S. Wainwright (J. A. M. A. 103: 1357 (Nov. 3) 1934) has noted that atrophic arthritics show skin sensitivity to stock and autogenous bacterial preparations and views a strong degree of inflammatory response as reflecting an etiological relationship.

On the other hand, J. C. Gittings (Wkly. Roster and Med. Digest. 29: 1127 (May 19) 1934) regards the relation of streptococci to the etiology of rheumatism in children as uncertain, emphasizing the fact that many individuals may develop sensitivity to streptococcal products, whereas only a few develop rheumatism. W. Bauer, G. A. Bennett and C. L. Short (New England J. Med. 208: 1035 (May 18) 1933) found no constant relationship of skin sensitivity to organisms in arthritic patients and doubt that skin sensitivity tests provide any sound basis for evaluating the etiological significance of a given organism.

Another indirect line of study has been applied recently by W. K. Myers, C. S. Keefer and W. F. Holmes (J. Clin. Investigation 14: 119 (Jan.) 1935) based upon the fact that the plasma of persons with known hemolytic streptococcus infections is more highly resistant to fibrinolysis than is plasma of normals and patients with other infections. Atrophic arthritis does not appear to be accompanied by an increase in the anti-fibrinolytic property of plasma.

Finally, J. A. Key (South. M. J. 26: 1059 (Dec.) 1933) has reported a failure to induce a chronic nonpurulent polyarthritis by inoculation of several streptococci. Many different sorts of mechanical injury, chemical irritants and interference with circulation have been shown to induce arthritic changes in joints. J. A. Key (J. Bone and Joint Surg. 13: 725 (Oct.) 1931) found hypertrophic arthritic changes in knee joints following surgical removal of sections of cartilage. G. A. Bennett and W. Bauer (*Ibid.* 17: 141 (Jan.) 1935) encountered hypertrophic arthritic changes following displacement of patellae. J. A. Key (*Ibid.* 15: 67 (Jan.) 1933) observed that injection of weak solution of acids, salts and alkalis, ink and even water into joints is followed by arthritic changes largely of hypertrophic character. A. Brunschwig and L. D. Henry (Arch. Surg. 27: 1065 (Dec.) 1933) have demonstrated that filtrates of cultures of *Streptococcus viridans*, *B. subtilis* and *diphtheroid bacilli* injected into joints at short intervals produce mild inflammatory reactions, as do likewise egg white and

human blood serum. Such lesions appear to be due to direct irritation effect of the proteins rather than to allergic phenomena.

J. F. Rinehart (Cited by R. L. Cecil J. A. M. A. 103 1587 (Nov. 24) 1934) has produced joint lesions similar to those of atrophic arthritis by intracutaneous injection of virulent streptococci in guinea-pigs on a vitamin C free diet. This observation, indicating a reciprocal relationship of seed and nutritional soil as a conditioning factor in the etiology of the disease, although as yet unconfirmed, is in principle at least in line with much clinical suspicion. Venous congestion has been seen to induce arthritic changes by M. A. Bernstein (J. Bone and Joint Surg. 15.661 (July) 1933). W. Bauer (New England J. Med. 208.1035 (May 18) 1933) considers that obstruction to lymph flow may also play a rôle in the etiology of joint pathology.

The importance of *age* as a factor influencing the type of arthritis has recently received considerable emphasis. The view has been advanced by A. D. Goldhaft, L. M. Wright, and R. Pemberton (Ann. Int. Med. 6 1591 (June) 1933) that the same precipitating factor may lead to atrophic arthritis when imposed upon young tissues, whereas hypertrophic changes ensue when imposed upon older tissues. This hypothesis is suggested on the basis of the finding that in old dogs cutting off the blood supply to the patella leads to hypertrophic changes, whereas the same operation in young animals is followed by less or no hypertrophic lesions.

The view that hypertrophic arthritis is largely conditioned by age is supported by F. Parker, Jr., C. S. Keefer, W. K. Myers, and R. L. Irwin (Arch. Path. 17.516 (Apr.) 1934), whose study of a series of 100 knee joints of 67 males and 33 females at necropsy indicated that even in the absence of clinical arthritis, most of the joints of persons beyond mid-life exhibited histological changes of hypertrophic arthritis. The lesions were found to be exaggerated and conditioned by trauma, hemorrhage, infection or urate deposits. The following data indicate the distribution of hypertrophic changes according to age:

None of 6 cases from 1-29 years,
66 per cent of 6 cases 30-39 years,
100 per cent of 9 cases 40-49 years,
95 per cent of 20 cases 50-59 years,
100 per cent of 28 cases 60-69 years,
94 per cent of 19 cases 70-79 years,
91 per cent of 12 cases over 80 years.

It is evident, in the light of these studies, that the response of joints to many different sorts of influences may lead to changes of arthritic nature and these, indeed, appear to conform to clinical experience which indicates that not one but many factors must be taken into account.

**Pathology.**—The practical utility of dividing chronic arthritis into 2 main varieties is almost universally recognized. This division is based primarily upon the differences of the pathological processes that dominate the joint picture. While recognizing the existence of such divisions some recent studies and reevaluation of older observations have been focussed upon some of the exceptions which do not fit into a rigid mutually exclusive differentiation. R. L. Knaggs (Brit

J. Surg. 20:113 (July), 309 (Oct.) 1932; 20:425 (Jan.) 1933) presents the view that both types are expressions at opposite ends of the scale of a single disease. The measure of vitality of the joint tissues in terms of their resistance to toxic influence is viewed as the deciding factor in the evolution of atrophic and hypertrophic arthritis. Further cogency is added to this point of view in the light of the fact that occasionally some joints pass from one picture to the other and in a few instances one joint appears to be typically atrophic while another in the same individual shows the hypertrophic picture. In a fair proportion of clinical cases it is often necessary to use the nondescriptive term of mixed arthritis.

*Atrophic Arthritis*—Allison and Ghormley (*loc. cit.*) have recently reaffirmed the fact that most cases of chronic arthritis can be definitely categorized on the basis of histological studies. These authors, in addition to noting the well recognized essential features, have emphasized the uniform appearance of focal collections of lymphoid cells in the proliferating synovial membrane and in the bone-marrow. This pathological feature is considered to be pathognomonic for proliferative (atrophic) arthritis. These writers point out that lymphocytes are incapable of participating directly in the destruction of the joint, whereas accumulations of polymorphonuclear leukocytes which occur in some arthritides lead to joint cartilage destruction by chemical means. The destruction of cartilage is entirely due to proliferative changes in the marrow and the synovia.

*Hypertrophic Arthritis*—In addition to the series of changes that have been described as characterizing hypertrophic arthritis, Allison and Ghormley mention the fact that the synovial membrane exhibits a moderately vascular structure, with fibrosis and more or less edema. In contrast with the membrane in atrophic arthritis, there is rarely any collection of lymphocytes.

In the light of the observation noted by C. S. Keefer, and W. K. Myers (J A M A 102 811 (Mar 17) 1934) that degenerative changes are almost universally present in persons beyond mid-life, the view of Allison and Ghormley that clinical hypertrophic arthritis is largely the result of traumata, is shared by many other students. Such traumata may be acute but are usually chronic micro-stimuli applied over long periods of time. Over-use of the joints, particularly of incongruous articulations, is viewed as the principal factor. While these processes are important, clinical data already cited indicate that rigid commitment to this concept of single and essentially specific etiology and nature does not appear to be justified.

*Dynamic Pathology.*—The story of pathological processes which may be reconstructed directly from the morphology and histology of joint tissues at section is at best incomplete, even as regards the joints themselves. While serial observations in a progressing case might reveal the sequence of the still pictures, they do not provide alone the data necessary to understand the nature of the influences which bring about the changes. In order to approach some conception of the latter, consideration should be given to the development, nutrition, physiology and function or metabolism of tissues involved. Attention is directed then, not only to the physiology of the joint tissue, but the physiology and

metabolism of the various systems that appear to be involved in this systemic syndrome.

Further data indicating a frequent disturbance of total rate of *metabolism* have been reported by F. C. Hall and R. T. Monroe (J. Lab. and Clin. Med. 18:439 (Feb.) 1933), showing that 50 per cent of 108 hypertrophic cases had basal metabolic rates below —10 and 18 per cent. below —15. These observations, like those previously cited, are obviously to be interpreted as showing a physiological trend and not to be considered as of diagnostic or prognostic importance.

*Nitrogen metabolism*, particularly purine metabolism, has often been considered to be disturbed in the arthritic. There is little or no recent evidence to support the view that there is any specific deviation of the metabolism of purines in arthritis. There is, furthermore, no extensive data to indicate that any of the phases of nitrogen metabolism are specifically altered. It should be noted that wasting or atrophy of muscular tissue which is often seen in severe cases of atrophic arthritis is associated with a loss of nitrogen from the body. The anemia which is a frequent feature is presumably associated with a slightly negative nitrogen balance. The degeneration of collagenous tissue and the increased formation of fibrous tissue are likewise evidence of local derangements of nitrogenous metabolism.

Mention has already been made of the appearance of antibodies, agglutinins and precipitins which represent modifications of the normal serum proteins induced by the presence of foreign proteins. In the same category, the high level of *fibrinogen* in atrophic plasma may be mentioned. There is some evidence to indicate that the total plasma proteins are slightly reduced in some cases. The latter factors represent nonspecific responses on the part of the individual to many different stimuli, but they may, in turn, exert an influence upon metabolism, *e. g.*, upon efficiency of circulation in capillary beds, upon the formation of edema.

*Carbohydrate metabolism* may be altered in arthritides, but this does not appear to be due to any deficiency on the part of the arthritic to burn sugar. B. D. Bowen (Personal Communication) reports that the respiratory quotient of the arthritic fed upon a high carbohydrate diet for a short period is normal. H. A. Nissen and K. A. Spenser (New England J. Med. 210:13 (Jan. 4) 1934) has observed a decreased rate of glucose removal especially among hypertrophics. W. Bauer (J. A. M. A. 104:1 (Jan. 5) 1935) found arteriovenous sugar curves that show a separation at the peak which is less than that seen in normals. These data confirm the impression that the deviations seen in glucose tolerance tests are probably secondary to circulatory changes.

The lipid *metabolism* has not been extensively considered. Statistical analysis of plasma cholesterol reported by Hartung<sup>39</sup> shows that hypertrophics have a significantly higher average level.

*Inorganic salt metabolism* is altered evidently in connection with the loss of calcium salts in the atrophy of bones, but this is not reflected in the level of calcium or of phosphorus in the blood serum. E. F. Hartung (Am. Assoc. Study and Control of Rheum. Dis., Cleveland (June) 1934), W. Bauer (*loc. cit.*),



and also C. W. Scull (Unpublished Data) in the writer's laboratory.) There are no gross differences from the normal level of the enzyme phosphatase among arthritics (H. L. Jaffe and A. Bodansky (Arch. Int. Med. 54: 88 (July) 1934); C. W. Scull, R. Pemberton (Unpublished Data); J. Race (Arch. M. Hydrol. 10: 6 (Jan) 1932). Meager data available indicate no gross deviation of the total base in sera.

Some recent studies have revived interest in *sulphur metabolism*, which was studied many years ago by R. Pemberton (Am. J. M. Sc. 144: 474, 1912) No constant changes in total sulphur metabolism were found to be related to the clinical course of the disease. A. P. Cawadias (Acta rheumatol 6: 26 (Feb-May) 1934) has presented data indicating a negative balance of sulphur in atrophic arthritis. J. Race (Lancet 2: 142, 1927), as far back as 1927 noted a relatively decreased rate of oxidation of sulphur. M. X. Sullivan and W. C. Hess (J. Bone and Joint Surg 16: 185 (Jan) 1934) have observed a decreased content of cystine in the finger nails This observation is confirmed by several workers Whether this is to be interpreted as a specific deficiency or as an expression of local nutritional inadequacy secondary to decreased blood supply to the finger nail awaits further investigation B. D. Senturia (J. Lab. and Clin. Med. 19: 1151 (Aug) 1934) has found no change in the glutathione content of either atrophic or hypertrophic blood.

The *acid-base* balance is not significantly altered insofar as is shown by the carbon dioxide capacity.

M. I. Sparks and R. L. Haden (Am. J. M. Sc. 184: 753 (Dec) 1932) have reported that atrophics have a relatively higher *blood plasma volume* than do normals and hypertrophics have a lower volume. These data signify to these authors that there is a pooling of blood in the splanchnic area C. W. Scull and R. Pemberton (Ann. Int. Med. in press) have shown that during recovery many patients lose water from the body This data is considered to indicate that active arthritis is associated with a low-grade edema The mobility of the swelling, stiffness and pain of the arthritic may be related to the ebb and flow of tissue water While the correlation of reduced tissue swelling with water loss is most evident in atrophic cases, the same measured loss of fluid often follows the change in the clinical state of hypertrophic arthritis

There is some deviation evident in the balance of the output of the *hematopoietic system* and the *blood destroying units*, as shown in the relative anemia which marks both types of arthritis and in the slight leukocytosis and "shift to the left" which occurs, particularly in the atrophic variety, as shown by W. B. Rawls, B. J. Gruskin and A. A. Ressa (J. Lab. and Clin. Med. 19: 830 (May) 1934) and by O. Steinbrocker and E. F. Hartung (J. A. M. A. 100: 654 (Mar. 4) 1933).

Considerable data have been adduced indicating that the *sedimentation rate* is elevated in atrophic and moderately so, if at all, in hypertrophic arthritis This physico-chemical phenomenon is generic to several diverse clinical states, evidently reflecting in a measure an increased relative concentration of fibrinogen While this may represent a nonspecific response of the plasma protein generating

organs to infectious processes, it should be borne in mind that pregnancy, presumably through metabolic stimuli, brings about a similar state in regard to the suspension stability of the red blood cells. In spite of these limitations imposed upon interpretation, empirical analysis indicates that the application of this determination may be useful in differential diagnosis of doubtful cases and in following the course of progress. The technic should include corrections for the relative anemia, as in the procedures of M. M. Wintrobe and J. W. Landsberg (Am J M. Sc. 189.102 (Jan ) 1935) or M. D. Rourke and A. C. Ernestine (J. Clin. Investigation 8:545 (June) 1930)

The variability of *skin function* previously noted, as reflected in change of skin temperature and variations in the skin capillaries, has been confirmed by J. Kovacs (J A M A 100 1018 (Apr 1) 1933), who has utilized photographic technic for recording the appearance of capillaries. The most marked deviations from normal appear in the regions of involved joints. While further investigation is necessary to determine whether the changes seen in the skin parallel changes in the blood flow in the articular structures, the observed changes are encountered with such frequency that they should be considered as part of the dynamic pathology of the extraarticular tissues at least.

Dysfunction characterizes other systems of the body. The *gastrointestinal function* is disturbed as indicated by the frequent finding of hypochlorhydria, colonic stasis, and atony of the musculature of the colon. Poor posture obviously imposes handicaps upon the function of circulatory, respiratory and gastrointestinal function. Although the metabolic nature of the frequently encountered fatigue remains obscure, there is a functional involvement of the *nervous system*. The nature of the dynamic changes characterizing the *muscular, connective and bony tissues* of the arthritic likewise remains obscure, although the consequences of such changes are evident even to a superficial observer.

The development and function of *joint cells* have been studied with tissue culture technic by E. Vaubel (J Exper Med 58 63 (July) 1933), who finds that the synovial cells are related to chondroblasts and osteoblasts, and that they exhibit polymorphism. The growing synovial cells secrete mucin, whereas their transformation to fibroblasts is accompanied by a loss of this function. H. B. Fell (Arch. J exper Zellforsch 7:390 (Oct 12) 1928) as far back as 1928, noted that cartilage cells are formed from mesenchyme. The chondrogenesis which takes place in the absence of blood supply is followed by ossification which is characterized by the formation of reticular fibrous tissue rather than hematopoietic tissue.

C. S. Keefer, W. K. Myers and W. F. Holmes, Jr (Arch Int Med 54 872 (Dec.) 1934), have recently summarized some of the factors involved in the physiology of *synovial fluid*. The data indicate that the synovial fluid is a transudate from the blood of noncolloidal electrolytes mixed with mucin secreted by the synovial cells. Those factors increasing transudation are held to result in an increased volume of fluid. For example, increased quantities of joint fluid are associated with increased venous pressures in cases of congestive heart failure, with decreased plasma proteins in nephrotic edema, and with obstructions to lymphatic drainage in thrombophlebitis of the femoral vein. The fluids in

such cases possess a low protein and low cellular content, as compared with the effusions occurring during the course of inflammatory processes, which are rich in protein and cells.

The importance of adequate *lymphatic drainage* of joints in the maintenance of a normal fluid volume is emphasized by W. Bauer, C. L. Short and G. A. Bennett (J. Exper. Med. 57:419 (Mar.) 1933), who have demonstrated by precipitin tests that molecular aggregates of the size of globulins are removed *via* the lymphatics. The rate of removal of such injected material can be accelerated by passive movement or by massage of the tissues adjacent to the joint. Inflammation has been shown by J. G. Kuhns (Arch. Surg. 27:345 (Aug) 1933) to decrease the rate of absorption of particulate matter from the joint cavity. Lopez has demonstrated by the x-rays that the rate of removal of lithium chloride from the joint may be materially reduced by various kinds of obstruction to the lymphatics.

The transportation of *crystalloid substances* to joints from the gastrointestinal tract that has been noted, is further amplified by J. G. Kuhns and H. L. Wetherford (J. A. M. A. 103:1883 (Dec. 15) 1934), who have demonstrated that intragastric administration of colloidal dyes is followed by intraarticular deposits of the dye *via* the reticulo endothelial system.

The *synovial fluid* has been shown by W. F. Holmes, C. S. Keefer and W. K. Myers (J. Clin. Investigation 14:124 (Jan.) 1935) to possess a chloroform soluble antitryptic substance. Polymorphonuclear leukocytes increase the activity of this substance, which is apparently derived from the blood. This antitryptic substance inhibits the action of autolysates from pneumococcal and staphylococcal exudates which alone cause rapid digestion of cartilage *in vitro*. A chemical as well as a mechanical protective function must then be ascribed to synovial fluid.

J. A. Key (South M. J. 26:1059 (Dec.) 1933) has presented evidence to indicate that the surgical removal of section of joint cartilage is often followed with hypertrophic changes. W. Bauer and G. A. Bennett (J. Bone and Joint Surg. 17:141 (Jan.) 1935) have emphasized the etiologic importance of patellar displacement incident to the operation. These latter authors consider that the friction generated by the patella over the lesions inhibits the rate of repair and that the hypertrophic lesions are primarily due to *traumata*.

Attention is again directed to the data indicating that the joint tissues respond to many different sorts of apparently unrelated agents or irritants with the production of degenerative and proliferative changes.

**Symptomatology.**—Except for the few features of clinical pathology mentioned above in the previous section, there is little to add to the description of the symptomatology of arthritis. Brief reference may be made to the existence of a low-grade *edema* of extraarticular tissues which, in the view of C. W. Scull and R. Pemberton (*loc. cit.*), parallels in a measure the activity of the arthritic process in both types. This swelling is particularly evident in the soft tissues of the dorsum of the hands. Early in the course of therapy, particularly along dietetic lines, these tissues present the appearance of relative collapse with “dimpling” and wrinkling of the skin. This reduced turgescence is often asso-

ciated with a diminution of pain and increased range of joint motion. The former event may precede the development of the latter changes

**Treatment.**—From the foregoing description of the nature of the disease it is evident that treatment of both types of arthritis must be conducted along several fronts. In the absence of any known single etiological factor, no one line of prophylactic therapy is possible. In view of the complex nature of disease, when once established, no single therapeutic measure is likely to prove adequate in all cases or in all stages of the disease even in the same individual.

Insofar as generalizations may be made, it appears that treatment should begin with those measures which contribute to the establishment of equilibrium of the major systems of the body at a level of "optimal physiology." The achievement of this depends upon a large number of specific features directed toward the correction of various aspects of dynamic pathology. The first, and perhaps the most effective measure toward this end, appears to be included in **systemic rest**. Bed rest, while superficially representing a single prescription, actually involves many physiological components. This fact may be recognized most readily perhaps in terms of physical considerations in regard to the reduced mechanical strain imposed upon weight-bearing joints, although equally significant influences are exerted upon the functional capacity of several systems. It is generally recognized that circulatory dynamics are relatively more efficient in the recumbent than in the erect posture, partly because of the fact that less mechanical work is required to circulate the fluid. Furthermore, there is a more equitable distribution of blood in certain capillary areas. Graphic evidence of the more efficient function of the circulatory system when in the horizontal position is seen in the decrease of dependent edema. There is an evident application of this component of rest to the low-grade edema in arthritis and to the disturbed capillary blood flow in the skin.

Similarly, the limited capacity for handling oxygen in terms of relative anemia and reduced vital capacity becomes adequate under the condition of bed rest, which reduces the total turnover of oxygen necessary. Bed rest likewise entails a reduced skeletal muscle tone and work, with a resultant decrease in the amount of catabolites, which can be more readily removed. By the same token, the physiological work of the nervous system is reduced. The direction of gravitational pull on the gastrointestinal tract is altered, with resultant improvement of function. The chief clinical symptom which represents the end-result of these deviations is fatigue. The metabolic readjustment incident to bed rest permits liquidation of the debt incurred by previously unbalanced activity.

It is evident that optimal physiology is not to be attained through the use of rest alone, important though this set of factors may be in making specific contributions to the patient's resources of defense repair and adjustment. Two other general prescriptions, each consisting of several components, are also to be considered in this connection, *viz*, nutrition and elimination of factors which tend to adversely affect the disease. Included in these categories are **dietetics** and **removal of foci of infection or sources of toxemia** and **reduction of strains** imposed upon joint structures.

The application of these principles provides the background upon which successful therapy is based. The use of individual or supplementary measures toward this end obviously entails due regard for their limitations as well as their potential for benefit.

Mention may be made of the status of **vaccine therapy** which, like other measures, may be evaluated in terms of its possible contribution to the above program. Views are at present divided as to the utility of these agents, however; almost without exception, they are advocated by their proponents as a part of the general reconstruction or the prophylactic program. Several points of view are held as to what vaccines should be used and as to the most appropriate routes of administration. The view that an exaggerated sensitivity exists on the part of the arthritic toward certain organisms or their products has led several investigators to consider that desensitization is an important desideratum. At the same time, the stimulation and production of protective antibodies is believed to be desirable. On the basis of experimental observations, it would appear that intravenous administration of vaccine might be expected to achieve these results. Hence, a number of workers advocate the procedure. Accordingly, J. C. Small (*Acta rheumatol* 5:26 (Dec) 1933) advocates administration of minute doses of a saline extract of streptococcus vaccine of organisms obtained from a case of rheumatic fever; Rawls, Gruskin and Ressa (*loc cit.*) autogenous strains of streptococci which cross-agglutinate with patient's own serum; Wainwright (*loc. cit.*), autogenous or stock strains to which the patient's skin is most sensitive. On the other hand, Nicholls and Stainsby (*loc cit.*) observed no difference between effects of stock and autogenous vaccines given subcutaneously or intravenously, and, furthermore, noted that the administration of vaccines did not appear to enhance the rate of improvement which followed surgical removal of foci alone. W. Bauer, G. A. Bennett and C. L. Short (*New England J Med* 208:1035 (May 18) 1934) present data indicating that skin reactions do not provide a reliable method for selection of an etiological organism.

In the light of these somewhat conflicting views, it is apparent that the use of vaccines is at present fraught with difficulty and at best their use should be subordinated to a broad program.

The list of so-called **antirheumatic drugs** probably includes hundreds of compounds. This large group of substances contains a few which possess useful and safe pharmacologic properties. No single one of them described to date, however, has been shown to restore to normal all of those physiological deviations which comprise the syndrome. While interest centers from time to time around old or new members of this list of agents, it is necessary to bear in mind the limitations of such agents.

Attention should be directed to the increased number of cases of liver damage which are recognized to follow the use of **cinchophen** and related compounds by certain patients who apparently become sensitized to these drugs.

There is a less hazardous, although none the less significant, limitation upon the use of **salicylates** which often aggravate, especially when used in injudiciously large amounts, the already present gastrointestinal dysfunction.

Mention should also be made of the dangers inherent in the intemperate use of various benzene derivatives as sedative, in view of the granulopenia which R. R. Kracke and F. P. Parker (Am. J. Clin. Path. 4: 453 (Nov) 1934) have seen to follow their use.

On the hypothesis that the disturbance in sulphur metabolism cited earlier can be corrected in part through the administration of sulphur, the use of drugs containing this element is advocated. **Colloidal sulphur** in various media are used, intravenous and intramuscular routes being utilized. Additional study is required to evaluate the place of this drug, although some limited experiences indicate that it possesses real therapeutic value in selected cases (Sullivan and Hess (*loc. cit.*))

The use of **gold salts**, **sodium aurothiomalate** and **calcium aurothioglycolate**, is advocated by J. Forestier (Lancet 2 646 (Sept 22) 1934) as a valuable chemotherapeutic agent, on the basis of favorable results seen following intramuscular injection. The dosage is given in amounts of 0.1 to 0.2 Gm ( $1\frac{1}{2}$  to 3 grains) until a total of 1.5 to 2.0 Gm (23 to 30 grains) is reached. The use of heavy metal salts is probably contraindicated in cases with cardio-renal complications. This measure needs further study for evaluation of its proper place in therapy.

The reduced peripheral blood flow has inspired a search for pharmacological as well as physical measures for increasing cutaneous blood flow. Two drugs have been used for this purpose, **histamine** (D. H. Kling Arch Surg 29 138 (July) 1934) and **beta-methyl-acetyl-choline** (J. Kovacs Am J M Sc 188 32 (July) 1934). Both substances are administered transcutaneously with the aid of the electric current. The former causes capillary dilatation with bleb formation and the latter arteriolar dilatation and stimulation of sweat glands. Both have been reported as providing symptomatic relief of pain in muscles and joints. The latter substance induces a response much like the physiological reaction following massage and, indeed, the latter may be really effected through the intermediation of a related substance, **acetyl-choline**.

**Magnesium sulphate packs** are helpful in allaying local pain. **Oil of wintergreen** applied locally sometimes helps achieve the same effect. This action is probably due to the transcutaneous entrance of salicylates.

P. S. Hench (Proc. Staff Meet., Mayo Clin 9 603 (Oct 3) 1934) has suggested that administration of **glycine** as a mild metabolic stimulant, particularly to muscles, may help relieve the sense of fatigue, especially in those cases in which myositis is a prominent feature.

The reports of P. S. Hench (*Ibid.* 8 430 (July 12) 1933) that analgesia accompanies attacks of jaundice have led to the use of **bile salts** in treatment. The value of this line of therapy awaits more extensive trial, particularly in view of the fact that an increase in circulating bile salts is not the only factor conceivably responsible for the effect observed.

**Physical Therapy**—Recent advances in physics have made possible the application of additional measures of physical therapy which may help correct the deviation in physiology or perhaps even directly destroy certain infectious agents. Most of these advances center around the application of radiant energy

with the production of heat in the tissues. The use of **infra-red radiation** from lamps or resistance coils permits somewhat deeper penetration of heat into the tissues than is possible with heated water or heated air.

The passage of a **high frequency current** through the tissues meets with resistance and hence heat is generated therein. This principle of **diathermy** is applied both locally and systemically. The passage of ultra short radio waves through tissue likewise produces a heating effect. This principle of **radiothermy** may be applied systemically or locally. All of these procedures have been used to provide a controllable fever. Temporary or permanent benefit has been alleged to follow such treatment on the premises already cited for the use of therapeutic fevers in general. These measures have been introduced too recently to permit of proper evaluation of their place in therapy. As with many new and powerful tools, uncritical use courts disappointment and disaster. Enthusiastic application of these agencies with the expectation of a "cure-all" and to persons too debilitated to withstand vigorous therapy, constitutes poor practice.

*Influence of Gastrointestinal Tract*—Changes in the colon, characterized by an atony of the muscular bands of the colon, have been recognized for some time. Other muscular tissue shows this decreased tone. Similarly, other parts of the gastrointestinal tract exhibit evidence of dysfunction. This atony may precede the disease, more or less parallel it or result from it, and, when present, may lead to various sorts of difficulty. It appears probable that among the secondary consequences of this derangement there may develop a nutritional inadequacy even in the presence of an otherwise adequate diet. Pemberton, Peirce and Bach have recently pointed out the possibility that the gastrointestinal tract may be the base from which transient invaders in the substance of bacteria may surge forth into tissues, including those of the joints.

*Diet*—The achievement of optimal physiology can be realized only on the basis of an optimal diet. The materials of metabolism must be supplied in appropriate kind and quantity.

While there is no experimental evidence indicating that arthritis is a specific deficiency disease, there is widespread recognition of the empirical fact that many, if not all, arthritics can profit by the ingestion of a well-balanced dietary both in terms of quality and quantity.

Pemberton, Peirce and Bach (*loc cit*) have demonstrated that arthritics may improve when placed upon experimental diets essentially deficient in vitamins. This, of course, does not mean that diets lacking in vitamin are recommended or even desirable, it merely suggests the possibility that other nutritional factors are involved. The present writers have shown that part of the change taking place during underfeeding or during periods of relatively reduced carbohydrate intake involves the state of hydration of the body as a whole. Under such circumstances, the body becomes relatively dehydrated. F. J. Sladen, D. C. Insign and C. M. McColl (*J. A. M. A.* 103: 1732 (Dec. 1) 1934) have made a statistical study of the composition of the diets voluntarily ingested by arthritics as compared with a group of nonarthritics. While they found the diets of the two groups to be essentially the same, the arthritics ingested only one-tenth to one-third of the carbohydrate from protective foods, and, furthermore, the increase

of the proportion of this fraction of the dietary led to significant constitutional changes, as reflected in joint and bowel function.

The estimation of an appropriate diet in a given case is not sufficiently well standardized to predicate accurately what the patient should eat. An approximation of the caloric value of the diet may be made by adding 10 per cent to the predicted basal heat production during 24 hours for a patient resting in bed. The diet should provide adequate protein, not less than 0.7 gram (11 grams) protein per kilo ( $2\frac{1}{5}$  lbs.) body weight, and should contain a variety of food-stuffs particularly high in the accessory food factors. This latter may be provided for by the liberal use of 5 and 10 per cent vegetables.

*Other Forms of Therapy*—A recent evaluation of the procedures for **sympathetic ganglionectomy** by M. S. Henderson and A. W. Adson (J. Bone and Joint Surg. 14: 47 (Jan.) 1932) indicates that this operation, of highly limited application to severe cases only, is most effective in young patients with patent arteries, vasospastic symptoms, including cold, wet, pale cyanotic extremities. The operation is of little value in advanced cases with ankylosis, infection, or with involvement of large joints and the results may be ephemeral.

The alleged similarity of some phases of arthritis to parathyroidism has led to the recommendation for **parathyroidectomy**. W. Bauer (*Ibid.* 15: 135 (Jan.) 1933) has, however, shown that there is little justification on the basis of metabolic studies for this operation.

Replacement therapy, advocated on the basis of supposed deficiency, has a limited range of application. The low basal metabolic rate and the similarity of some aspects of the joint lesions to those encountered in hypothyroidism have been cited as indicating the necessity for **thyroid** medication. The slow rate of removal of glucose has been cited as indicating an insulin deficiency. As noted earlier, however, actual carbohydrate combustion follows a normal course in arthritis. On other grounds, the use of **insulin** as a stimulant to appetite in emaciated and anorexic patients may be useful. The specific use of various **ovarian hormones**, particularly in cases of arthritis occurring in mid-life, appears at present to be founded on inadequate premises in view of the incidence of hypertrophic arthritis in men at the same age periods. So far as the menopause *per se* introduces its own train of events, however, these may serve to dislocate an existing equilibrium and so pave the way for arthritis or aggravate an existing arthritis. Amelioration of this situation, therefore, deserves consideration from this standpoint.



# Cardiovascular System

*by*

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**ANGINA PECTORIS.—*Etiology.***—ANEMIA.—A. H. Elliot (Am. J. M. Sc 187:185 (Feb.) 1934) reports the case of a 55-year-old woman with chronic anemia and repeated epistaxes who had attacks of angina pectoris over a period of 3 years which became extremely severe with the occurrence of a febrile illness. Necropsy showed the heart to be hypertrophied but otherwise normal. The coronary arteries were thin-walled and dilated, and detailed study revealed no lesion in their walls other than occasional flecks of lipoid on the intima; the aorta was unchanged. It is concluded that severe anemia, by increasing cardiac output, may cause myocardial hypertrophy, that under these circumstances the adaptive limit of the coronary flow may be reached in the resting state and easily exceeded under additional physiologic circulatory burden, and that the resultant myocardial ischemia might express itself as an anginal seizure.

Also, L. Bouchut and R. Froment (Arch. d. Mal. du Cœur 27:325 (June) 1934) point out that in cases of pernicious anemia with very low hemoglobin levels the weight of the heart is often moderately increased (to 400 or 500 grams, and occasionally more). The hypertrophy appears to vary directly with the severity and duration of the anemia, and, although the change has been most often seen in the pernicious type, secondary anemia, provided it is severe and prolonged enough, may give rise to it. The authors agree with those who have considered it a work hypertrophy. They also consider that the anoxemia of chronic lung disease may similarly increase the output of the heart and therefore its work, which fact might explain the cardiac hypertrophy sometimes seen in these conditions, especially when the hypertrophy affects both sides of the heart.

K. Paschke (Klin. Wchnschr. 13:767 (May 26) 1934) describes 4 cases of angina pectoris in severe anemia. In 3 instances, efficient treatment of the anemia led to disappearance of the angina for very considerable periods. 1 patient had pernicious anemia and auricular fibrillation, another, pernicious anemia with little objective cardiopathy; the third, secondary anemia from menorrhagia, with syphilitic aortic disease.

**TOBACCO AND ALCOHOL**—For years, the relationship of the use of tobacco and of alcohol to angina pectoris has been a topic for idle speculation. In view of this fact, P. D. White and T. Sharber (J. A. M. A. 102:655 (Mar. 3) 1934) have analyzed a series of 750 private patients with angina pectoris followed from 1921 to 1933, to determine the amounts of tobacco and alcohol habitually used prior to the development of the angina pectoris, and a control series of 750 individuals without angina pectoris and of exactly the same sex and age incidence and from the same walks of life. A somewhat higher percentage of total abstainers from tobacco was found among the patients with angina pectoris than among the individuals without angina pectoris (46.1 per cent as compared to 37.2 per cent) and a somewhat lower percentage of persons using much or an excessive amount of tobacco in the angina pectoris series than in the control series (24.4 per cent as compared to 33.5 per cent). From these figures the conclusion may be drawn that past habits of tobacco smoking are not primarily responsible for angina pectoris. The actual balance of "better habits" in favor of the individuals

who developed angina pectoris may perhaps be explained, as in the case of neurocirculatory asthenia, by their greater sensitivity to tobacco, which makes them avoid it altogether or, at least, in excess. Although the smoking of tobacco (especially cigarettes) is largely a "nervous habit," many nervous people do not use it. Occasionally, patients in the angina pectoris group either volunteered the information or responded to questioning that omission or reduction of tobacco was helpful by causing a decrease in the frequency of attacks of angina pectoris; rarely, patients ceased having attacks of angina pectoris altogether when they stopped smoking. Total abstinence from *alcohol* was the history of 64.4 per cent. of the cases of angina pectoris and of 61.7 per cent. of the control series. Only 8 of the 750 patients with angina pectoris (1.1 per cent.) drank considerable or excessive alcohol, while 63 (8.4 per cent.) of the control series drank much alcohol.

From this study, it appears that neither the use of nor the abstinence from tobacco or alcohol plays an important rôle in the genesis of angina pectoris. In occasional cases, the use of tobacco apparently aggravates or precipitates attacks of angina pectoris, and in occasional cases alcohol helps to prevent or to relieve such attacks.

**Treatment.**—In the management of patients with anginal pain, the physician is called upon to exercise all of the resourcefulness and tact which he possesses. As stated by R. L. Levy (New England J. Med. 211:392 (Aug. 30) 1934), attacks of discomfort referred to the sternum or left side of the chest may be associated with many different clinical states. The "angina pectoris" of Heberden is not a disease in the accepted sense, but a symptom whose cause must be carefully sought before treatment can be undertaken with reasonable hope of success.

The mechanism by which pain arises in the heart is as yet but imperfectly understood but it is believed to occur when the heart muscle does not receive an adequate supply of oxygen. Some of the clinical conditions which may be responsible for a derangement in the balance between the supply of oxygen and the demand for it by the heart have been outlined by Levy, as follows:

"1. *Disease of the coronary arteries.* This is the chief cause of anginal pain, for it induces a condition which properly might be called 'coronary insufficiency.' It may be due to

(1) Arteriosclerosis

(a) Slight, with patchy intimal sclerosis

(b) Marked, with calcification, and narrowing or obliteration of the lumen

(2) Syphilis of the aorta, with stenosis or occlusion of one or both coronary orifices

(3) Rheumatic arteritis, a rarer condition

"2. *Aortic insufficiency*, regardless of etiology. It is believed that the lowered diastolic pressure which accompanies this valvular defect results in an inadequate blood flow through the coronary system.

"3. *Anemia.* The heart suffers from anoxemia along with the rest of the body.

"4. *Hyperthyroidism.* The increased metabolic demands of the body require an increased velocity of blood flow and an augmented volume output by the heart. The added demands placed upon the myocardium may be greater than its capacity to increase its supply of oxygen.

"5. *Paroxysms of tachycardia.* Again, the rapid rate may call for a greater coronary flow than can be delivered.

"6. *Combined states.* For example, marked anemia occurring in an individual with coronary sclerosis will induce pain more readily, as a rule, than in a person with normal coronary vessels.

"Paroxysms of pain referred to the chest may be observed under other circumstances, and sometimes simulate the discomfort resulting from anoxemia, though not the result of it. Differential diagnosis is important, both for prognosis and therapy. Some of the conditions which may cause confusion are the following:

- (1) Psychoneurotic states.
- (2) Poisoning by tobacco or coffee
- (3) Aneurism of the aorta.
- (4) Pericarditis.
- (5) Arthritis of the spine, with resultant intercostal neuralgia.

"**APPROACH TO PATIENT.**—Any individual who has a pain in the region of the heart is alarmed. He thinks immediately of some acquaintance or relative who has died suddenly following a similar complaint and his first question is apt to be: 'Have I angina pectoris?' He wants, above all, reassurance. It is my practice, under these circumstances, to state at the outset, that there is no such disease as angina; that this term means merely a painful or uncomfortable sensation in the chest, and that it will be our aim to discover the nature of the condition which lies at the basis of the discomfort

"The diagnosis and estimation of the gravity of the situation will depend largely upon a carefully taken history. Notation of the normal habits of the individual with respect to work, recreation, sleep, food and exercise are essential, for they may require modification. Of particular significance is the patient's response to effort, in relation to his pain. Almost invariably, the same activities or series of events, if repeated day after day, result in the same type of discomfort. Minor inconsistencies in this relationship do occur as the result of modifying factors, such as fullness of the stomach or chilling. But when there are major discrepancies between inciting cause and painful response, the fault usually does not lie in the heart

"A complete examination, including electrocardiogram, x-ray and fluoroscopic examination of the heart, blood count and Wassermann test, serves further to determine the etiology and to define the nature and extent of the structural changes. When there is any question of thyroid dysfunction, the metabolic rate should be determined. In the presence of rheumatic heart disease, the rate of sedimentation of the red blood corpuscles may help in distinguishing between an active and an inactive lesion. At the conclusion of the survey, the patient should have the feeling that his condition has been thoroughly investigated. In the final analysis, the best estimate of the degree of functional derangement is obtained from the patient's own story

"The second question which naturally follows closely after the first is: 'What is my outlook for the future?' There are rare individuals who really desire a frank statement of the whole truth. But, as a rule, even those who stoutly assert that they 'want to know everything' prefer to hear an encouraging report. To dodge the issue or to lie is neither advisable nor necessary. A part of the truth, tactfully presented in simple language, is often all that is necessary to allay fear. It is fair to say that all of us, after the age of forty, are subject to changes in the arteries, which manifest themselves by loss of elasticity and the appearance of fatty or even chalky deposits. Such alterations may take place in the vessels or organs or tissues without interfering with function. If, however, there is hardening of the arteries of the heart, discomfort may ensue, even though the lesion is slight. There need be no discussion of a sudden accident with the patient, but a responsible member of the family should be fully informed as to the possibilities

"**MANAGEMENT OF PATIENT**—Where specific therapeutic measures are indicated, as, for example, in syphilis or anemia, the problem of treatment is clearly defined. But, by far, the greatest number of those who seek relief because of anginal pain are men between 45 and 60 years of age, in whom sclerosis of the coronary arteries is the source of the trouble. To modify existing lesions or to arrest the progress of arteriosclerosis, are accomplishments as yet beyond our powers. For the most part, therefore, it must be our endeavor to manage the

patient rather than to attempt to treat his disease. With his cooperation, there must be worked out a regimen which will make for comfort, for as much activity as possible, and for the prolongation of life.

"Attention to detail is imperative and determines, in large measure, the success or failure of the undertaking. Each individual presents his own peculiar problems, according to his temperament, station in life and daily habits. It is necessary, in spirit, to arise with him in the morning, go through a typical day and see him through a night's rest, in order to guide him in his course of action.

"In his activities, the patient must aim to live within the limits of his pain. Moderation is the watchword, but he should be permitted to have as full a life as his disability will allow. There are many men active in business or one of the professions who have carried out their best work after the onset of cardiac discomfort. Often, friends and associates are unaware of any limitations. A rest on a couch in the office, after lunch, may serve to break the day and enable a man to continue with the work of the afternoon. The ascent of stairs, where possible, should be avoided, for stair-climbing places a sudden demand upon the circulation. If a flight must be taken, it is well to have the patient pause between each tread.

"It is folly to forbid all exercise and the amount possible will vary in each instance, as well as in the same person at different stages of his illness. Violent games, such as squash or tennis, are not apt to be attempted because of their unpleasant effects. Golf on a level course, and horseback riding, are often possible when the myocardium is not severely damaged. It is well to advise the **avoidance of any form of exercise** for relaxation, **when already fatigued**. **Light general massage and resistance gymnastics**, according to the Schott method, may be tried in those who, by nature or force of circumstances, are physically indolent.

"The choice of *occupation* for patients who have gained a livelihood by manual labor presents a problem in sociology and economics, as well as one in medicine. With the severe grades of pain, the sufferer simply cannot carry on. Jobs as elevator operators for such as these are always at a premium. When the intellect permits, clerical work is sometimes possible. A traveling salesman can often be of use in the home office. A complete change in the character of occupation is difficult, particularly in these days of depression and unemployment. Where total disability exists, one of the surgical measures, later to be referred to, may be undertaken.

"The control of **diet** is sometimes the keynote of a successful regimen. Almost invariably, the patient will volunteer the information that he is more subject to attacks after a meal. The stomach should never be overloaded, and 5 small feedings are preferable to 3 large meals. If there are nocturnal attacks, the evening meal should be light, and taken early, with dinner in the middle of the day. The specific articles to be taken will vary with the nationality and social status. Flatulence, above all else, is to be avoided. The older writers, all stressed this point, and they were right. The members of the cabbage family, including brussels sprouts and cauliflower, as well as corn and cucumbers are taboo. Sweets and starchy foods should be taken sparingly. If diabetes or gout is present, suitable modifications must be made to care for these metabolic faults. Insulin, if necessary for the control of hyperglycemia, must be given with caution, for it causes an increase in the work of the heart and may induce an anginal paroxysm. Many of the older diabetics in whom coronary sclerosis is marked, do better without insulin even though their urine shows a faint reducing reaction and the level of the blood sugar is slightly elevated. The obese must be taught to reduce, but gradually and, above all, without the use of thyroid extract.

"Climatic influence cannot be disregarded. Many of these patients are more subject to attacks in the cold weather and, in the winter, fare better in a warmer atmosphere. Some, who can arrange to do so, prefer to live where the weather is more equable and temperate, as in California. To walk in the face of a blasting wind is to invite disaster.

"At least 8 hours in bed, at night, should be insisted upon. An occasional day or half day in bed is often useful in building up reserve. In the severe cases, a week or two spent in bed may result in permanent betterment.

"Before the interview has proceeded very far, the use of alcohol, coffee and tobacco will come up for discussion. Alcohol is sometimes helpful in relieving a paroxysm. Its continued use, in moderation, is often beneficial rather than harmful, for it induces peripheral vasodilatation and relaxation. In the obese, indulgence must be curtailed. A cup of coffee in the morning frequently acts as a bracer, and unless it is followed by discomfort, is to be allowed. A cup of weak tea in the afternoon likewise serves as a 'pick-up' for some. The attitude which the physician takes toward tobacco will vary. In general, patients with anginal pain are better off without it. For many, it is a poison and its use results in increase in the frequency and severity of attacks. There are those, however, who derive real comfort and emotional stability from smoking. In them, curtailment is urged and the de-nicotined cigars and cigarettes may be tried. The value of the de-nicotining process is open to question, but the patients themselves not infrequently think that they can smoke such brands with comfort whereas ordinary varieties are less well borne. Perhaps the reason for such experiences lies in the fact that the de-nicotined products, especially the cigars, contain milder tobaccos.

"The cultivation of an even temper is helpful. It was John Hunter who was accustomed to say that 'his life was in the hands of any rascal who chose to annoy and tease him.' And he died at a board meeting in St. George's Hospital following a fit of anger. Card playing, even for small stakes or for none, may cause pain in the emotionally susceptible. A tranquil bearing in the contacts of daily life can be achieved with the exercise of conscious effort. For those who suffer from nocturnal attacks, a quiet hour before retiring aids in securing undisturbed sleep.

"There are, on occasion, reflex factors which tend to lower the threshold of the heart for pain. Chief among these is chronic cholecystitis, either with or without stones. The removal of the infected gall-bladder may result in reducing both the number and severity of the attacks. I have recently seen 2 instances in which duodenal ulcer was present in patients who presented unmistakable evidence of coronary disease. In them, the anginal pains were much diminished by the institution of the Sippy regime, helped, no doubt, by a period of rest in bed. Constipation, both because it induces straining at stool and makes for the accumulation of the products of intestinal putrefaction, should be controlled by diet, as well as laxatives when necessary. Foci of infection in the teeth, tonsils and sinuses, in my experience, have seemed to play an insignificant rôle with respect to anginal attacks. On general principles, infected teeth, though not necessarily all dead teeth, should be extracted. In using a local anesthetic for this purpose, the dentist should be instructed to omit epinephrin from the solution which he injects, for it may readily induce a paroxysm. Tonsillectomy in patients with coronary disease, especially in the elderly, should be approached with caution and done only when the indications for it are urgent. Likewise, in treating chronic sinusitis, conservative measures should be given preference.

"The well-to-do patient is prone to favor a sojourn at a Spa, usually in the course of a trip to Europe during the summer months. I have never been able to convince myself that the medical measures carried out in these health resorts are superior to those commonly employed at home, nor that the various hydrotherapeutic procedures so frequently stressed produce any effect other than the induction of temporary peripheral vasodilatation. Perhaps the latter is desirable. On the other hand, I am frank to admit that several weeks spent at such an establishment often prove beneficial. The patient is away from home and free of care. The surroundings are pleasant and there is good music to be heard. The day is planned with proper regulation of activity and rest. The food is simple but well prepared. There are waters to be drunk which exert a mild laxative action. A pilgrimage has been made in the company of others. All these factors combine to react favorably upon one who is in a receptive and impressionable mood.

"**DRUGS**—An attack will sometimes subside within a few minutes following the cessation of activity or the calming of an excited nervous system. **Nitroglycerin**, upon which the sufferer soon learns to depend, was first used as a remedy for anginal pain by Murrell in 1879. In 1 per cent alcoholic solution, he gave it to 3 patients who experienced great relief. It is more conveniently carried as a tablet, which should be thoroughly chewed before swallow-

ing. A small dose (1/200 or 1/150 grain—0.3 or 0.45 mg.) often suffices and does not induce the flushing and headache which may follow the larger and more commonly used 1/100 grain (0.6 mg.) tablet. It is important to insist that nitroglycerin tablets be fresh and that they be used within 2 months of the date of manufacture. After the expiration of 6 to 8 weeks, their strength deteriorates. It would be well if the bottles containing such tablets were dated by the commercial drug firms. The odor of amyl nitrite, in the form of "pearls," makes it less popular than the nitrite in tablet form. When the attack persists for more than 30 minutes and is not relieved by nitrites, particularly if this is contrary to previous experience, occlusion of a coronary branch should be suspected.

"The value of **nitroglycerin** as a *prophylactic* is not sufficiently appreciated. It was Professor K. F. Wenckebach, of Vienna, who first called my attention to its use in this manner. If a tablet, or if necessary, two, be taken prior to anticipated physical activity or nervous strain, the effort can often be carried through to a painless conclusion. In this way, an executive may be enabled to preside at a board meeting, a lawyer to plead in court or a salesman climb an unavoidable flight of stairs. There is no harm in repeating the dose several times in the course of a day, if occasion demands it. The regular use of the nitrites, particularly those having a more prolonged action, such as erythroltetranitrate, is not to be recommended. The results are not so satisfactory as when necessity or prevention are the indications employed.

"Other drugs should be administered with a clear idea of what they are expected to accomplish. When congestive heart failure is present, **digitalis**, along with other appropriate measures, is employed. In some patients with enlarged hearts and a small cardiac reserve, the continued daily use of a maintenance ration, as emphasized by Christian, is often helpful in preventing frank cardiac insufficiency. In certain instances, on the other hand, digitalis appears to aggravate the severity of the pain and to cause more frequent recurrence of paroxysms. Under these circumstances, obviously, it must be discontinued.

"Mild sedatives, by producing a more equable state of mind, and by lowering the threshold for pain, are frequently beneficial. **Phenobarbital** or the **bromides** serve well in this capacity and may be given, in small doses, continuously or intermittently, over long periods of time. A **soporific** at bedtime may avert nocturnal seizures, and a drink of **spiritous liquor** before retiring sometimes accomplishes the same end.

"Various preparations have been tried which are said to induce dilatation of the coronary arteries and thereby augment the flow of blood through the heart muscle. Of these, **aminophyllin** (theophyllin-ethylene-diamin) has enjoyed the widest popularity, and certain patients claim that they feel better when taking it. In a dose of 0.1 Gm. (1½ grams), it is dissolved in water, and is taken 3 or 4 times daily. Theobromin, theophyllin-calcium-salicylate (**phyllicin**) and theobromin-calcium-salicylate (**theocalcin**) have also been used. In my hands, various organ extracts, such as those marketed under the trade names of 'myorgal', 'padutin' and 'angioxyl' have proved worthless.

"The number and intensity of anginal paroxysms are subject to wide variations over a period of months or years, in the same individual. Often discomfort increases, but occasionally the attacks become less numerous and milder, occurring only after unusual exertion or an intense emotional experience. They may even disappear completely. The patient learns to adapt himself to his malady, his nervous system becomes more stable, and perhaps compensatory adjustments take place in the coronary circulation. Under such variable conditions, and when judgment of the therapeutic result must be based entirely upon the individual's account of his subjective experience, a just appraisal of the value of any particular medication is difficult. A recent study was made in the Cardiac Department of the London Hospital, designed to throw light on this very point.\* After giving some 15 different preparations to 90 ambulatory patients, with a placebo regularly substituted for an active drug, the authors were unable to convince themselves, after 2½ years of observation, that any drug was worthy of trial in routine treatment.

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\* W. Evans and C. Hoyle. *Quart. J. Med.* 2: 311 (July) 1933.



"**SURGICAL MEASURES.**—There is a small group of individuals who suffer intensely from anginal pain and who, after trying faithfully all of the measures which have been outlined, including rest in bed, continue to find life burdensome. For this limited number, surgical therapy may be undertaken, with the clear understanding that there is no question of altering the basic pathologic state; the aim of treatment is purely the relief of pain.

"In America, **cervical sympathectomy** for this purpose is no longer common practice. It has been tried and found to be neither rational nor effective. Section of those dorsal roots carrying painful impulses from the heart does indeed abolish discomfort. It is a difficult technical procedure involving laminectomy and requiring a long session on the operating table. It has been performed successfully in a few cases.\* But in the presence of severe coronary disease, such an undertaking is not to be undertaken lightly. The one patient in whom I have seen the operation attempted, while under the anesthetic, developed a thrombus in the left coronary artery just as the surgeon was about to make his incision, and died 12 hours later.

"The **paravertebral injection of alcohol**, if skilfully done, is practically devoid of operative risk. In a series of 26 cases under my observation at the Presbyterian Hospital, Dr. Richmond L. Moore has carried out this procedure without mishap. After a review of the literature and a survey of the records of our own patients, it appears that complete or great relief of pain may be expected in approximately 50 per cent, some degree of relief will be obtained in another 30 per cent; and in 20 per cent, the injections prove to be entirely without benefit† The operation must, of necessity, be done without the aid of visual guidance. The ability to deposit the alcohol in the vicinity of the small rami communicantes is probably the largest factor which determines success or failure, and this will vary with the technical dexterity of the surgeon. If relief was afforded, the effect has lasted for as long as 3 years, and may be permanent. The most troublesome complication has been painful intercostal neuritis, which has resulted from the infiltration of the intercostal nerves with alcohol. This has persisted for as long as 8 weeks. It is apparently, at times, unavoidable, due to the close proximity of the various nervous structures at their point of exit from the spinal canal.

"There need be no fear of eliminating pain as a danger signal given out by the heart. Almost invariably, a substitution symptom has appeared—dyspnea, a sense of clutching in the throat or substernal oppression—which has served as a guide to the patient. Such substitution symptoms are promptly relieved by **nitroglycerin**. The patients generally know from their own experience how much they may safely do.

"During the past year our Boston colleagues, who first suggested total **thyroidectomy** as a therapeutic procedure, have been accumulating information concerning its effects‡. It is their idea that with a lowered metabolic rate, the cardiac output and the velocity of blood flow are lessened and so a lighter load is placed upon the heart. An impaired coronary circulation, inadequate for the needs of a normal metabolic rate, will carry sufficient oxygen for the myocardium which is functioning at a lower level. The reported results are indeed encouraging. Our own experience is too limited to permit of an expression of opinion. Longer periods of critical observation will serve to assign to thyroidectomy its proper place in treatment.

"In conclusion, it is well to stress again the importance of a complete analysis of each case. This should include not only a consideration of the medical problem, but the social, economic and personal aspects as well. It is not within our power to abolish, or indeed significantly to modify, those physical disorders which are responsible for anginal pain. Moderation, tempered with optimism, will bring comfort to many, for some, in spite of limitations, there will be possible a long and fruitful life. For the rest, there must be solace in the words with which Sir William Osler, almost forty years ago, ended his lectures on

\* L. Davis. J. A. M. A. 101: 1921 (Dec. 16) 1933.

† R. L. Levy and R. L. Moore. Arch. Int. Med. 48: 146 (July) 1931.

‡ H. Blumgart, S. A. Levine and D. Berlin: Arch. Int. Med. 51: 866 (June) 1933.

'Angina Pectoris and Allied States' 'Terrible as are some of these incidental conditions accompanying coronary artery lesions, there is a sort of kindly compensation, as in no other local disease do we so often see the ideal death—death like birth, "a sleep and a forgetting".' "

**AORTIC STENOSIS.—Etiology.**—A definite history of *rheumatic infection* was obtained in 23 per cent. of the autopsied cases and in 46 per cent of the clinical series observed by S. McGinn and P. D. White (*Am. J. M. Sc.* 188:1 (July) 1934). The latter series included another 32 per cent with a questionable rheumatic history. Important intercurrent infections were found in the histories of about one-third of the postmortem cases and nearly one-half of the clinical cases, which incidence probably varies but little from that in the population at large. It has seemed to the authors likely that a severe *tonsillitis*, with or without peritonsillar abscess, in youth or middle age may be an etiologic factor in the origin of aortic valve disease found in middle life or old age without mitral valve disease and without a history of rheumatic fever. Nonsyphilitic aortic regurgitation was encountered in several cases of this type developing in males of middle age. Syphilis was not diagnosed in any case of the clinical series and in only 4 cases of the postmortem series. Of the postmortem series, 54 had had their Wassermann reactions tested and in only 3 were they positive. The diagnosis of subacute bacterial endocarditis was made on 6 occasions in the clinical series, but was found only twice in the postmortem series. Sixteen of the total 123 autopsied cases (13 per cent.) were judged on gross examination to be Monckeberg's sclerosis of the aortic valve. None of these cases had a positive history of rheumatic infection. No cases of congenital aortic stenosis or subaortic stenosis were encountered in the postmortem series nor, as far as could be ascertained, in the clinical series. The known duration of the lesion, as well as could be determined, was 9.5 years for the postmortem cases and 12.7 years for the clinical cases up to the present time or until the time of death.

**Pathologic Anatomy** — In the postmortem series McGinn and White (*Ibid.*) made a comparison of cases showing *calcareous* changes in the stenosed aortic valve with cases without calcareous change. Calcareous valvular changes were found more frequently than noncalcareous (86 to 37), with males predominating (4:1) and living past middle life in the calcareous group, while in the noncalcareous group the sexes were evenly distributed and few lived longer than 50 years. Angina pectoris, cardiac asthma, and higher blood-pressure were more frequently found in the calcareous group, while a positive rheumatic history and auricular fibrillation were more frequent in the noncalcareous group. The average pulse pressures were approximately the same. The heart weights were similar in the two groups, averaging 616 grams in the calcareous group and 579 grams in the noncalcareous group, but calcareous changes in the mitral valve, aorta, and coronary arteries were much more common, as would be expected, in the older, calcareous group. The presence or absence of calcareous changes in the aortic cusps is clinically relatively unimportant as compared to the aortic stenosis itself, excepting as it alters the degree of stenosis or aids in the x-ray diagnosis.

A comparison of the autopsied cases having *aortic stenosis combined with mitral stenosis* showed males to be represented equally in both groups; females,

however, were 3 times more frequent in the combined than in the isolated group. Mitral stenosis was found much more often in the cases dying under 50 years, while aortic stenosis alone occurred most commonly in people beyond that age. Angina pectoris was found more often in patients with aortic stenosis alone (14 to 2), while auricular fibrillation occurred much more often in cases with complicating mitral stenosis (26 to 13). The average heart weights were approximately the same for the two groups (612 grams and 592 grams respectively). Coronary sclerosis and aortic sclerosis were more common in the cases of aortic stenosis alone; sclerotic changes in the mitral valve were found in 23 of the 50 cases with complicating mitral stenosis.

In 3 groups of patients of the postmortem series presenting various degrees of calcareous aortic stenosis, it was found that the correct diagnosis had not been made clinically in any having only moderate calcareous changes, mostly at the base of the aortic cusps, and that the symptoms of congestive failure were less frequent in this group than in cases where the lesion was more marked. At least a few of the cases showing only a moderate aortic stenosis should have been diagnosed correctly antemortem if proper attention had been directed to the signs that were present. The patients with pronounced aortic insufficiency in addition to aortic stenosis had a shorter terminal illness and died at a younger age than did the cases where stenosis of the valve predominated. The average weight of the hearts in the group with pronounced aortic insufficiency (685 grams) was also higher, the smallest hearts (450 grams) being found in those cases with little or no aortic insufficiency and with only a moderate amount of stenosis.

McGinn and White conclude that all grades of aortic stenosis exist, much as in the case of mitral stenosis; that aortic stenosis even of considerable degree is common, particularly in males, that it is doubtless often caused by infection, especially rheumatism, that calcareous changes are found chiefly in the older patients, no matter what the etiology, that aortic stenosis is less serious than aortic regurgitation of high degree, being found in many old patients after years of valvular disease, that it is sometimes associated with considerable hypertension, that, as in the case of mitral stenosis, the symptoms and signs vary in number and degree with the extent of the aortic stenosis, that aortic stenosis is often overlooked when it should be clinically diagnosed, and that it is an important lesion to search for, even in the lesser grades, because of the progression of the lesion and of the frequency with which it is associated with congestive heart failure.

**Symptoms and Signs.**—The complaints of the patients were chiefly those of congestive failure, and were found mostly in the histories of the autopsied patients where diagnosis of congestive failure had been most frequent. Faintness, dizziness, or actual syncope were also fairly common complaints, having been found in 22 per cent of the histories of the combined series of 236 cases. The clinical diagnosis of aortic insufficiency was made frequently in both series; clinically diagnosable aortic insufficiency was present in 52 of the autopsied cases and in 74 cases of the clinical series. Angina pectoris was found in 47 patients (19 per cent.) and cardiac asthma in 36 patients (15 per cent.)

All of the clinical cases had loud systolic murmurs at the base of the heart, almost all of which were accompanied by systolic thrills. A basal systolic murmur was recorded in half the patients of the postmortem group and a basal systolic thrill in one-fourth. Physical examination very often showed a harsh systolic murmur transmitted over the entire precordium, which was frequently attributed antemortem to a mitral lesion. Wide transmission of the systolic murmurs to the neck and back was recorded in a few records. The aortic second sound was either diminished in comparison with the pulmonic second sound or entirely absent in a majority of the patients, this finding being more common in the autopsied series where the cases of congestive failure were more numerous. Not rarely, however, the aortic second sound was found to persist even in the presence of well-marked aortic stenosis, later proved at postmortem examination. The pulse was described as normal or full in the majority of the patients, a Corrigan pulse being noted in 12 cases of the entire series of postmortem and clinical cases; a plateau pulse was reported in 9. The systolic blood-pressure was 150 mm. of mercury or over in 65 patients (of the total of 236 of both groups); the majority of diastolic pressures varied between 80 and 110 mm. mercury; the average pulse pressure was 60 mm., unexpectedly high. Only 10 of the total number of cases failed to show cardiac enlargement to the left by either percussion or x-ray examination. Infrequently the calcified aortic valves could be seen in fluoroscopic examination, and rarely they could be demonstrated by teleroentgenography.

**Diagnosis.**—In the last two generations the requirements for establishing the clinical diagnosis of aortic stenosis have approached the extremes. When a basal systolic murmur alone permitted a diagnosis of aortic stenosis, the lesion was diagnosed too frequently, while, on the other hand, the more recent extreme point of view has minimized the frequency of the lesion and may be considered over-cautious in requiring for diagnosis the following criteria: (1) loud aortic systolic murmur; (2) aortic systolic thrill, (3) absent aortic second sound, (4) plateau or anacrotic pulse; and, by some, (5) an aortic diastolic murmur.

According to S. McGinn and P. D. White (*Ibid.*), the preferable diagnostic position lies between these extremes. At times the diagnosis may be justified in the presence of a harsh and loud aortic systolic murmur transmitted to the neck, whether or not it be accompanied by one or all of the signs of a confirmatory nature, such as an aortic thrill, absent aortic second sound, a plateau pulse and aortic diastolic murmur. In the presence of other valvular deformities or of a history of rheumatic infection, and in the absence of syphilitic aortitis or of marked hypertension, a loud systolic murmur in the second right interspace should strongly suggest aortic stenosis. In a review of 6800 necropsies of patients with all types of disease at the Massachusetts General Hospital, they found 123 cases (1.8 per cent) of aortic stenosis, and in a clinical group of 4800 patients seen in cardiovascular practice, 113 cases (2.3 per cent). \* The stenosis demonstrated at autopsy was diagnosed clinically in only  $\frac{1}{3}$  of the cases. In the post-

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\* In a study of 1000 English ex-service men with signs of acquired cardiovascular disease, R. T. Grant (Heart 16:275 (June) 1933) found, after 10 years of observation, 43 individuals with aortic stenosis and regurgitation without mitral stenosis and 6 others who had both aortic stenosis and regurgitation with mitral stenosis.

mortem series, 71 per cent. of the patients were males, in the clinical series, 63 per cent.

**CORONARY ARTERY DISEASE.—*Pathology and Incidence.***—In a statistical analysis of the autopsy and clinical records of 762 cases of coronary artery disease (observed at the Presbyterian Hospital, New York City, during the period 1910 to 1931), made by R. L. Levy, H. G. Bruenn, and D. Kurtz (Am. J. M. Sc. 187: 376 (Mar.) 1934), *arteriosclerosis* was the most common lesion, being present in 97.2 per cent. of the cases. Syphilis did not play a rôle in predisposing to coronary sclerosis. It was present no more frequently in patients with coronary disease than in those without it. Syphilitic aortitis, by inducing stenosis or occlusion of the coronary orifices, was responsible for impairing the coronary blood flow in 5.7 per cent.

In 2877 consecutive autopsies, lesions of the coronary arteries were found in 25.9 per cent. (a strikingly high figure). In one-half of the cases showing sclerosis in the coronaries, the lesions were "slight" or "moderate"; in many of these instances, no functional impairment of the cardiac circulation was induced by such relations. The lesser degrees of sclerosis were observed predominantly in the younger groups; the more marked lesions developed with advancing years.

In this series of autopsies, the incidence of coronary disease showed a slight, but steady, increase throughout a 22-year period; but the increase was not nearly so great in the proven cases as was indicated by the figures based on clinical diagnosis alone, which fact may be explained chiefly by the decline of infectious diseases and the aging of the population. The much greater rise in the frequency of the clinical diagnosis of coronary disease is due in large measure to altered fashions in terminology and to sharpened clinical acumen. As stated by Levy in 1932 (Am Heart J. 7: 431 (Apr.) 1932, also SUPPLEMENT to the CYCLOPEDIA, p. 219, 1933), physicians have become not only "heart-minded," but "coronary conscious." There has been an increase at all ages, particularly noteworthy between the ages of 25 and 44, with a predominance of males. Occupation does not appear to play a significant rôle in determining those whose vessels were affected. The largest percentage was found among foremen and skilled workers. Many cases are latent and, possibly, cannot be recognized during life. During the years 1920 to 1931, even in the presence of calcification or stenosis, the diagnosis was made clinically in 16 per cent. of the cases, and coronary thrombosis was correctly diagnosticated in only 43 per cent. of the cases. The most frequent primary cause of death was arteriosclerotic heart disease; and cardiac insufficiency was the commonest terminal event. The increase in the incidence of affections of the coronary arteries is not to be regarded as a matter of concern, rather, should it be a source of satisfaction that, due largely to effective control of infectious diseases, men may survive to an age when disorders incident to senescence lead to the termination of life.

**ATHEROSCLEROSIS.—*Pathogenesis.***—In a study of the origin of human atherosclerosis by T. Leary (Arch. Path. 17: 453 (Apr.) 1934), the lesions of human atherosclerosis were reproduced in the rabbit by the feeding of cholesterol. Rabbits, 5 months old when the experiment started, were fed cho-

lesterol by catheter for a maximum period of 7 months. For the first 4 months, starch paste was used as a menstruum, the pure cholesterol being finely powdered before suspension; for the remaining 3 months sunflower seed oil was substituted as a menstruum, the cholesterol being dissolved (1 Gm to 20 c c) in warm oil. A limit of tolerance at about 1 Gm of cholesterol *per diem* was established.

**HUMAN CORONARY SCLEROSIS**—According to the histologic changes present in fatal cases of human coronary sclerosis, Leary divided the subjects into 2 groups. In the first group, represented by persons 25 to 55 years of age, the dominant change in the coronary arteries consists of *fibrosis leading to narrowing of the lumen*. In the second group, represented by individuals from 47 years to extreme old age, the dominant change consists of collections of lipoid cells with a tendency to atheromatous necrosis, giving rise to so-called *atheromatous "abscesses"*. The lesions in the first group represent a reaction of youth, while the lesions in the second group depend apparently on a lack of this reaction at older ages.

*Group I*—The nutrition of the *new fibrous tissue* depends in its early stages on imbibition from the blood circulating in the lumen. Ultimately, as the fibrous layer increases, this becomes inadequate and necrosis results. The internal elastic lamina in the advanced processes (in the terminal conditions) showed fragmentation and flattening, even disappearing in regions where the fibrous layer had crossed its site and invaded the media. Only occasionally was there evidence of reduplication. While conditions of stress favor the localization of lesions in the arteries, definite morphologic evidence of injury to the elastica is not constant. Varying degrees of local invasion of the media by connective tissue were found. In this group varying degrees of lymphoid cell infiltration of the intima were seen, in 6 of 8 cases there was no lymphoid cell infiltration of the media in the left coronary artery (the favorite region of localization of atherosclerosis in its most extreme form), in 1 there were focal collections of cells, and in another diffuse infiltration, perivascular collections of lymphoid cells occurred in the adventitia of all of the coronary arteries, with exception of 2 cases. Studies of early processes in branches of the coronary arteries, where the lesions were still proliferative and without necrosis, revealed no lymphoid cell invasion or other evidences of inflammatory reaction. The relation of the lymphoid cell infiltration to the advanced lesions, in which necrosis had occurred, makes it probable that the inflammatory reactions arise in this disease as a response to the presence of necrotic tissue products. The inflammatory reaction is, therefore, secondary and usually late. Tangible deposits of lime salts did not occur in the coronary arteries of the first group. Lipoid cell groups, usually small, were found in all of the coronary arteries in this group and definite atheromatous regions of liquefaction were present in the coronary arteries of 4 cases. In all of these vessels the intimate relation of lipoid cells to the new growth of fibrous tissue was manifest, being best illustrated in early lesions in the smaller branches of the coronary arteries. The author believes that fibrinous or fibrinoid necrosis arising in the subendothelial tissues and extending to the intima is the lesion which leads to



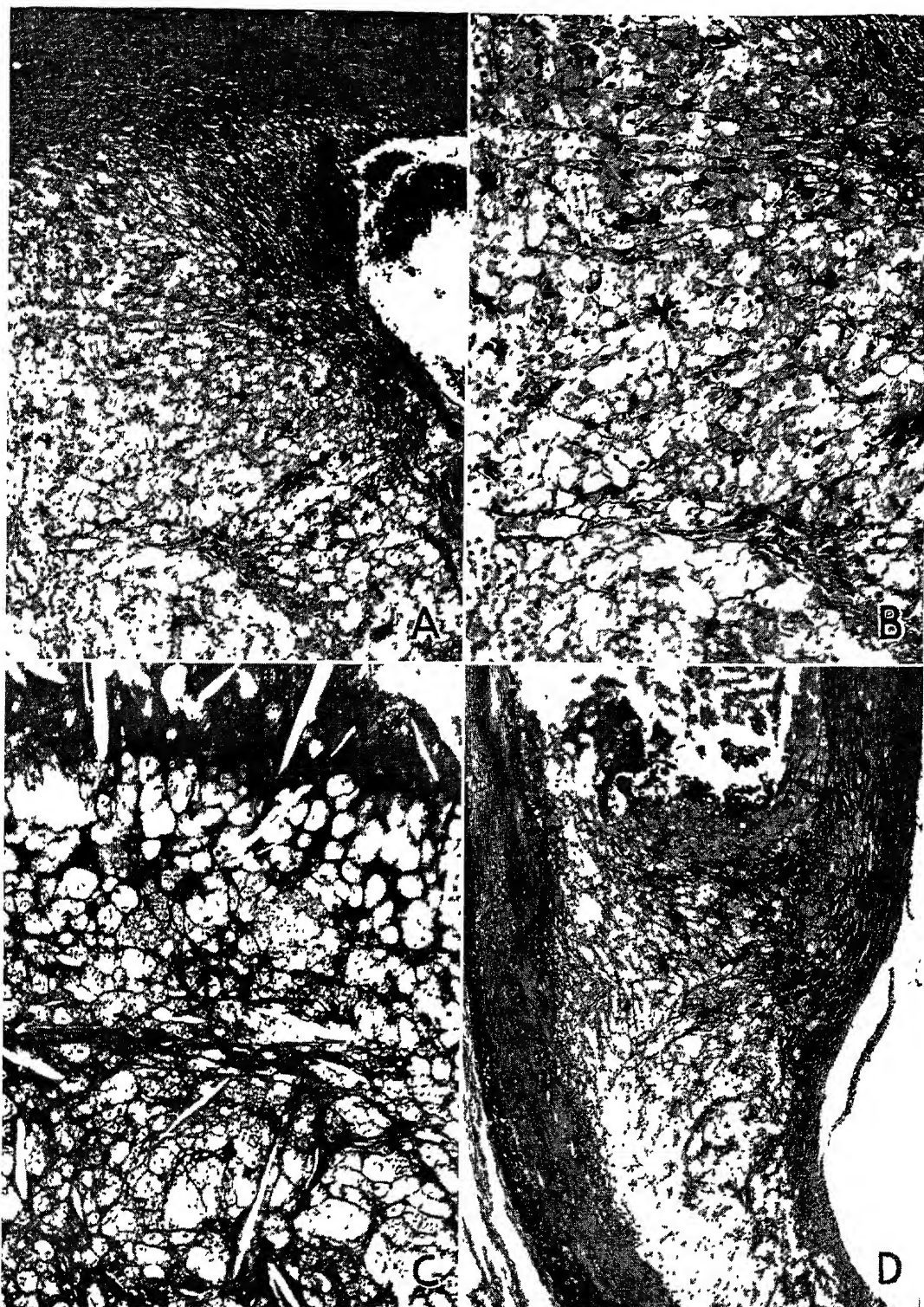


Fig 1—Human coronary arteries showing evolution of atheromatous "abscess" (A) Lipoid cell masses near lumen,  $\times 100$  (B) Detail of lipoid cell masses,  $\times 175$ . (C) Necrotic lipoid cells with splitting of lipoid esters,  $\times 200$  (D) Atheromatous "abscess,"  $\times 76$  (T. Leary. Arch Path)

engulf the cholesterol esters and give rise to the most characteristic element in human or in experimental sclerosis, *i. e.*, the large macrophage loaded with lipid esters in fine or coarse droplets. As the disease progresses, the lipid cells become massed in the subendothelial connective tissue. In the experimental form, the layers of cells, large globular structures, may be multiplied into hillocks which distort the lumen of the vessel. The cells are separated by delicate partitions of connective tissue, though more than one cell may occupy a compartment in the connective tissue (Fig. 2).

As the process ages, it is common to find deeper invasion by some of the lipid cells as fibrosis of the inner layers takes place. When lipid cells accumulate, even in isolated groups, necrosis of the cells tends to occur. The early stages are marked by the breaking down of the cytoplasm and the fusing of the esters which have existed in fine droplets, into larger drops. This is followed by the splitting of the esters and the freeing of cholesterol in crystal form. A rare lesion in the rabbit is the atherosclerotic cavity, or "abscess" (Fig. 3).

The standard progressive change in the rabbit is fibrosis. When the accumulation of lipid cells has reached a certain degree, young fibroblasts appear and replace the cells. This replacement is total, including the lipid cells, their contents and the supporting tissue. It is unaccompanied in general by the splitting of the esters, though occasionally small deposits of cholesterol crystals are found. In both rabbit and man the formation of fibrous tissue is more frequently diffuse than local, the delicate strands between the lipid cells becoming thicker as the lipid cells disappear. The result of fibrosis, which tends to progress *pari passu* with the occurrence of lipid cells, is formation of fibrous cells distorting and narrowing the lumen of the vessel. From the comparative study of human and rabbit atherosclerosis it is seen that the fibrosis which is characteristic of human coronary lesions in the young is the characteristic lesion in cholesterol atherosclerosis in young rabbits. Therefore, fibrosis is a reaction of youth and not of species. The evolution of the lesions through lipoidosis, lipid cell formation and fibrosis, more rapidly produced in experimental animals, can be followed in greater detail in these animals than in human lesions, in which progress is so slow that the stages in the progression are distinguished with difficulty.

Recent human experience in diabetes supports the experimental findings in rabbits following cholesterol feeding. During and following the period when diets excessively rich in fat were used in the treatment of diabetes an increase of atherosclerosis was observed. Permanent storage of sugar, one of the most soluble and combustible food substances, does not occur in the body, while cholesterol is not combustible, its avenues of excretion are limited, and it tends to be stored. The inheritance of a poor cholesterol metabolism appears to be associated with the tendency to an early death from coronary sclerosis. As far as is known no cholesterol is synthesized by the human body, all of the supply is ingested. The most urgent demands for it come at times of most rapid cell formation. The high blood cholesterol found in pregnant women marks the mobilization of this substance for the needs of the fetus *in utero*. Man is the only animal that ingests eggs and milk throughout its lifetime, and, as far as is known, is the only animal



which dies in early life from coronary sclerosis, and which acquires atherosclerosis almost universally in advanced life.

**CORONARY OCCLUSION, ACUTE.**—*Treatment by Oxygen.*—

After sudden occlusion of a sizable coronary branch, anoxemia of the myocardium occurs, with consequent general oxygen want, which may be relieved by the inhalation of oxygen in high concentration. In 1930, A. L. Barach and R. L. Levy (J. A. M. A. 94:1363 (May 3) 1930; SUPPLEMENT to the CYCLOPEDIA, p. 247, 1932) called attention to the therapeutic value of oxygen in coronary

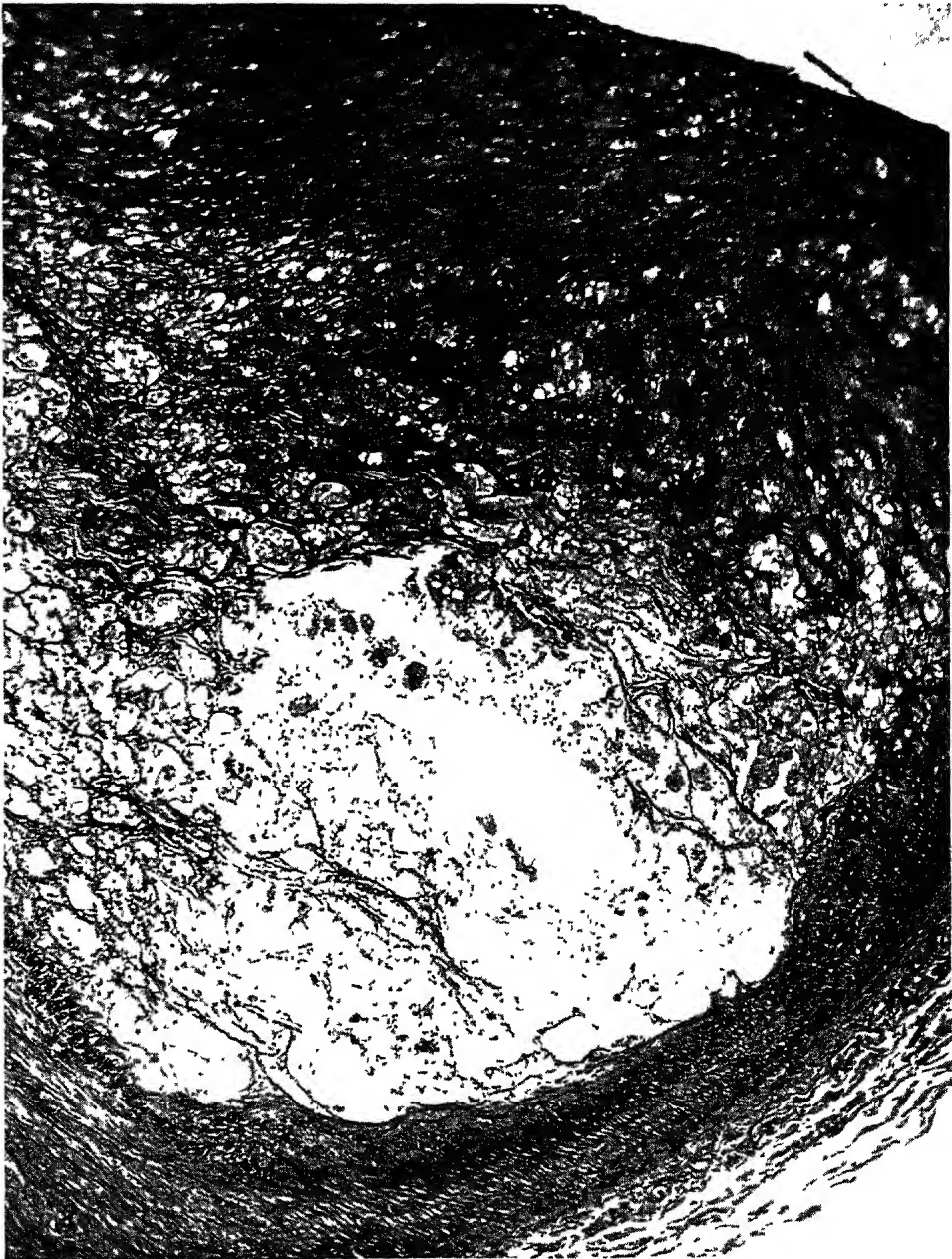


Fig 3—Innominate artery of rabbit,  $\times 100$ , atheromatous "abscess"  
(T Leary Arch Path)

thrombosis. A study of 16 new cases (J. A. M. A. 103:1690 (Dec. 1) 1934) has confirmed their earlier impressions, which may be summarized as follows

"1. Subjective improvement occurred in from 1 to 3 hours after the administration of oxygen was begun. The relief of pain was striking. Respiration became less labored and slower. The patient was no longer restless. It was therefore possible to curtail materially or even stop entirely the use of morphine and other sedatives

"2. Cyanosis was diminished or abolished

"3. Cheyne-Stokes breathing, if present, gradually disappeared.

"4. The temperature, in cases in which it was elevated, tended to fall.

"5. The heart rate became slower. The heart sounds grew stronger and the volume of the pulse improved. The signs of congestion in the lungs became less marked. As the state of circulation improved, the arterial blood-pressure rose and the venous pressure fell

"6. Interruption of oxygen therapy before adequate readjustment of circulatory conditions had taken place resulted in recurrence of the symptoms and signs just cited."

All these beneficial effects might not take place in every case. When one of the larger vessels is occluded, particularly if the heart muscle is already seriously damaged, recovery may not be possible. However, improvement might be effected in cases which seemingly offer little hope of a favorable course. In other patients, a sudden turn for the worse might result in death at a time when the prognosis seemed good.

*Method of Oxygen Treatment*—The presence of cyanosis is the classic index of oxygen want. However, at times an ashen gray color or pallor may be observed even in the presence of relatively severe anoxemia since capillary constriction, due to shock, may prevent sufficient blood from reaching the skin to transmit the bluish tint. The clinical picture is the best guide. Rapid heart rate, feeble heart sounds, often with gallop rhythm, labored breathing, persistently low blood-pressure and moist rales at the bases of the lungs are signals of distress from a failing circulation which needs support.

"The most effective way of giving oxygen is by means of a large, well-ventilated tent. The temperature inside the tent should generally be kept between 60° and 65° F., since at these levels most patients experience the greatest comfort. A concentration of 50 per cent oxygen is usually employed, 60 per cent can be given indefinitely without harm. In severe cases with rapidly progressive failure, 70 per cent concentration may be used for several hours at a time. Mixtures containing over 70 per cent are not recommended except for brief periods, for in animals such high concentrations have been found to be irritating to the lungs when administered continuously for a number of days. The aim of therapy is to maintain a degree of concentration sufficient to overcome the existing anoxemia.

"On the average it is desirable to keep the patient in the tent for about 5 days. This period may be shortened or extended, depending on the condition. It must be borne in mind, however, that the satisfactory and comfortable appearance of the patient may be due to the sustaining effect of inhaling a mixture rich in oxygen. For this reason it is advisable to lower the oxygen concentration gradually from 50 to 35 per cent over a 24-hour period, then to 21 per cent during the following 12 to 24 hours. If it is desired to stop oxygen without previous lowering of the concentration, the patient should be carefully observed, after removal of the tent, for signs of dyspnea and cyanosis. The pulse and respiratory rate should be counted at 15-minute intervals for 3 hours. If the heart rate does not increase more than 10 beats a minute above its rate in the tent, and the respiratory rate does not rise more than 6 a minute, oxygen may be discontinued. If such an acceleration in either cardiac or respiratory rate should occur, it is safer to continue treatment for another day and then stop the oxygen, the same observations being made.

"An oxygen chamber is, of course, a more comfortable method of therapy, but it is available only in a hospital. A portable chamber, made of rubberized fabric, can be brought to the home and affords a sense of greater spaciousness. It is more troublesome to set up and more costly to maintain.

"If a tent or chamber is not available, the nasal catheter may be employed as a measure of moderate effectiveness. The oxygen should come from a high-pressure tank and be given through a calibrated gage at the rate of from 5 to 6 liters a minute. This provides about 38 per cent oxygen, if the patient breathes through the nose. By placing the catheter beyond the posterior pharynx, so that the tip rests just above the glottis, Wineland and Waters (Arch. Surg. 22: 67 (Jan.) 1931) have found that a flow of from 7 to 8 liters per minute is capable of maintaining a concentration of 50 per cent. This is the rate of flow ordinarily employed in supplying a tent. A few patients that we have treated by this method complained of irritation of the throat, and a hacking cough necessitated withdrawal of the tube. The method is undoubtedly of value, but the throat must be sprayed frequently with liquid petrolatum."

The authors conclude, as in their 1930 paper, with these words:

"Employment of oxygen therapy may aid in maintaining an adequate circulation until the heart has had an opportunity to recover from its acute functional disturbance. Obviously, the cardiac injury may be so severe that recovery is impossible. But in certain instances, effective use of oxygen may be responsible for the saving of life."

**DIGITALIS.—DIGITALIS GLUCOSIDES.—***Comparison of Purified Glucoside and Whole Leaf Preparations.*—The selection of the most effective digitalis preparation is a problem which constantly confronts the medical practitioner. In recent years, through the realization that infusions and tinctures of the drug might fail in giving full therapeutic effect because of incomplete extraction of the active principles, preparations of the powdered whole leaf of digitalis in tablet, capsule or pill form have become more widely used. This trend has resulted in part from the recommendations of the Digitalis Committee of the American Heart Association. Also, during the last few decades, there have appeared a number of special preparations containing only the active principles—the glucosides—of digitalis, claimed to be capable of effecting full therapeutic benefit in dosage more accurately measurable. In an effort to determine whether or not there is any difference in the therapeutic value of whole leaf as compared with a purified glucoside preparation of digitalis, W. D. Stroud, A. W. Bromer, J. R. Gallagher and J. B. Vander Veer (Am. J. M. Sc. 187: 746 (June) 1934) studied a group of 25 ambulatory patients with established auricular fibrillation in the Adult Cardiac Clinic of the Pennsylvania Hospital. These patients were divided into 3 similar groups: one group was given a preparation of the extracted purified glucosides of digitalis, another was given a whole leaf preparation manufactured by a well-established pharmaceutical house, and the third group received whole leaf tablets prepared by the American Heart Association. The groups were followed clinically for 9 months, and then, after interchanging the preparations, for another period of 6 months. Bioassay of the preparations showed that the American Heart Association whole leaf tablets and the whole leaf preparation manufactured by the pharmaceutical house contained less than 1 cat unit each and, compared with 2 tablets of the glucoside preparation as 100 per cent, were 70 per cent. and 89 per cent. as potent, respectively.

At the completion of the study, no striking difference was observed in the general clinical picture, including the ability to work, of the members of the 3 groups. However, during the course of the study, before the summarization of the results and before the bioassay, it was the impression of the authors that the preparation of the extracted purified glucoside was somewhat more effective per *stated* unit of dosage than either of the two whole leaf preparations. Final analysis of the data tended to substantiate that idea, since in 5 (25 per cent) of the 20 cases given the purified glucoside preparation the daily maintenance dosage, measured in cat units, was smaller than that of either of the whole leaf preparations. This result may be explained by the relatively greater strength of the purified glucoside tablet as revealed by the bioassay. No difference was detected in the dosage per cat unit of the two whole leaf preparations. Since the bioassay revealed a greater potency per unit of dosage in the case of the purified glucoside preparation, it was impossible to determine whether the slightly smaller cat unit dosage necessary with this preparation, in a few cases, was the result of this factor or of better absorption, better fixation in the heart muscle or a combination of these factors.

**VERODIGEN.**—Verodigen, the *gitalin* glucoside of digitalis, first isolated by Kraft in 1912, has been used in Europe for a number of years with apparently good clinical results. As the preparation is generally unknown in the United States, a study of its biological action and therapeutic value has been made by W. D. Stroud, A. E. Livingston, A. W. Bromer, J. B. Vander Veer and G. C. Griffith (Ann. Int. Med. 8: 710 (Dec.) 1934).

As nondesiccated powder, at room temperature, verodigen is stable 20 months or more; it is soluble in water, bitter to taste, and has no definite melting point. Biologically, it is about 130 times as potent as standardized dry digitalis leaf. It is promptly absorbed from the small intestine of cats and dogs and, when so absorbed in large doses, about 50 per cent of the effect is present the next day. It produces vomiting which, in cats and dogs, is not due to local gastric irritation, inverts the T-wave of the electrocardiogram of dogs, slows the heart of cats and dogs, and stops the hearts of frogs and cats in systole.

The *clinical* study of its therapeutic efficiency was made upon (a) 5 patients with established auricular fibrillation and 1 patient with auricular flutter, previously untreated with digitalis, (b) 2 patients with regular sinus rhythm and advanced congestive heart failure, (c) 14 patients with established auricular fibrillation, previously controlled with whole leaf digitalis preparations or digalen. It was found (a) to control the ventricular rate in established auricular fibrillation, (b) to produce clinical improvement, with marked diuresis, in patients with congestive heart failure and regular sinus rhythm, and (c) to produce in the electrocardiogram S-T interval and T-wave changes, characteristic of digitalis action. Careful clinical observation revealed  $\frac{1}{240}$  gram (0.27 mg.) of verodigen to be equivalent to 1 cat unit (approximately  $1\frac{1}{2}$  grams of powdered digitalis leaves). The total dosage necessary for optimum digitalization varied from  $\frac{1}{10}$  to  $\frac{1}{16}$  gram (6 to 4 mg.), administered over a period of 5 to 6 days. The most frequent adequate maintenance dose was  $\frac{1}{240}$  grain (0.27 mg.) daily. Toxic effects from overdosage were similar to those produced by whole leaf digitalis.

preparations. The authors stress the fact that the *potency* of verodigen demands careful observation in its administration, especially with patients who have recently been taking any digitalis preparation.

**DYSPNEA.—MITRAL STENOSIS.**—In a study of 20 cases of mitral stenosis with attacks of acute pulmonary congestion with or without cardiac asthma, made by S. McGlinn and P. D. White (Am. Heart J. 9·697 (Aug.) 1934), 10 were uncomplicated and 10 were complicated by factors (aortic valve disease or hypertension) causing strain on the left ventricle. All of the second group had cardiac asthma, while 5 of the former had definite wheezing, the other 5 having severe paroxysmal attacks of dyspnea with hemoptysis or pink, frothy sputum, but without a clear history of wheezing. The average ages of the two groups when last heard from were 31·3 and 50 years respectively, half of the patients of the second group being over 50 years of age, whereas none of the first group had reached their fiftieth year. These figures should be contrasted with those in the series of 272 cases of cardiac asthma of all etiologies, recently reported by the same authors (New England J. Med. 207·1069 (Dec 15) 1932; SUPPLEMENT to the CYCLOPEDIA, p. 172, 1934), 90 per cent of whom, or 246 patients, were over 50 years of age; 96 per cent (260 cases) of that series showed no mitral stenosis, and so may be compared with interest with the present series of 20 cases with mitral stenosis (Table I).

TABLE I  
ACUTE PULMONARY CONGESTION  
*A Comparison of Cases With and Without Mitral Stenosis*

	Mitral Stenosis Without Cause For Left Ventricular Hypertrophy	Mitral Stenosis With a Lesion to Cause Left Ventricular Hypertrophy	Cases of a Former Series Without Mitral Stenosis
Number	10	10	260
Sex, Males	6	7	196
Females	4	3	64
Cardiac asthma	5	10	260
Number who have died	4	8	232
Number over 50 years of age	0	5	239
Average age at onset of attacks	26	47	58
Duration since onset of attacks to last report of living patients	3·5	6·5	4·1
Average age at death or last report	31·3	50	59·6
Duration in years from onset of attacks to death	3·9	1·9	1·6
Rheumatic history	7	6	11
Attacks brought on by exertion	8	7	23
Attacks brought on by coitus	3	2	
Attacks brought on by paroxysmal tachycardia	5	1	
Frank hemoptysis	7	1	50
Frothy sputum	7	6	70
Mitral insufficiency	3	8	5
Aortic stenosis and insufficiency	0	4	8
Aortic insufficiency	0	3	48
Hypertension	0	5	167
Angina pectoris ..	0	4	44
Auricular fibrillation	3	3	29

Eight of the 10 patients with mitral stenosis complicated by hypertension or aortic valve disease in the present study died after an average duration of life of 1.9 years from the first attack of asthma. The average duration of life of 4 patients with uncomplicated mitral stenosis who have died was 3.9 years from their first attacks of pulmonary edema to death. Two of these 4 patients died during attacks of pulmonary edema and the other two died after progressive myocardial failure. Exertion was the factor precipitating the attacks of acute pulmonary congestion in 7 of the 10 cases with mitral stenosis plus strain on the left ventricle and in 8 of the cases with pure mitral stenosis. In the general series of 272 cases of cardiac asthma without mitral stenosis, only 23 (8 per cent.) had attacks initiated by exertion, the vast majority occurring while the patient was in bed and at rest during the night; of those 23 patients, 3 had rheumatic mitral disease; 5, luetic aortitis; 4, arteriosclerotic coronary disease; and 11, hypertension. Five of the uncomplicated cases of mitral stenosis suffered pulmonary congestion with the onset of attacks of paroxysmal tachycardia.

Only 1 of the 10 cases with complicated mitral stenosis suffered frank hemoptysis in contrast to 7 of the 10 uncomplicated cases, while the presence of frothy sputum was noted 6 and 7 times respectively in the two groups. Angina pectoris coexisted with cardiac asthma in 4, and auricular fibrillation in 3 of the patients with mitral stenosis and left ventricular hypertrophy, whereas none of the 10 patients with uncomplicated mitral stenosis had angina pectoris, and 3 had auricular fibrillation. Left ventricular hypertrophy was present in all the cases having hypertension or aortic disease associated with the mitral stenosis. X-ray examination was made in 8 of the other 10 cases, and all showed "mitral-shaped" hearts with enlarged left auricles and prominence in the region of the pulmonary cone. In 4 of these cases there was general enlargement of the heart, but it was thought to be of right-sided origin, and in no case was left ventricular enlargement noted. Neither of the remaining 2 cases of uncomplicated mitral stenosis showed enlargement of the heart to the left by percussion in the fifth intercostal space.

It seems, therefore, that in the large group of cases with *left ventricular strain and failure*, acute pulmonary congestion is found in older persons; comes on most often while the individual is at rest; has a poor prognosis, but may be successfully treated for a while with digitalis and diuretics. In these cases, the acute pulmonary congestion very likely results from a backing up of blood in the pulmonary vessels, due to the inability of the left ventricle to expel its full contents.

In cases of *uncomplicated mitral stenosis*, acute pulmonary congestion is found in younger individuals; the attacks are precipitated by exertion or paroxysmal tachycardia, and are often accompanied by frank hemoptysis, the prognosis is more favorable than in most other cases of cardiac asthma, although digitalis and diuretics are of less value. According to the authors, the best explanation of the acute pulmonary congestion in these cases is that when the heart is stimulated to greater work, the hypertrophied and dilated right ventricle propels more blood into the pulmonary vessels than can pass through the stenosed mitral valve in the same unit of time, with a consequent acute pulmonary congestion. In cases of mitral stenosis associated with an enlarged and dilated left ventricle

due to systemic hypertension or to an aortic valve lesion, it may be assumed that either or both of the mechanisms just described may be effective.

**NOCTURNAL DYSPNEA.**—In a clinical study of 30 patients with cardiac disease subject to attacks of nocturnal dyspnea, W. G. Harrison, Jr., J. A. Calhoun, and T. R. Harrison (Arch. Int. Med. 53:561 (Apr.) 1934) found the following to be precipitating and predisposing causes of the attacks: (1) the recumbent position of the body in 27 cases, (2) cough in 23 cases, (3) the amount of activity engaged in during the preceding day in 21 cases, (4) abdominal distention in 17 cases, (5) large evening meals in 12 cases, (6) constipation and the desire for bowel movements in 12 cases, (7) hunger in 8 cases, (8) unpleasant dreams in 8 cases, (9) heat in 8 cases, and (10) urination in 7 cases.

The patients consisted of 11 white men, 4 white women, 8 negro men, and 7 negro women. The oldest patient was 68 years of age, the youngest was 23. Hypertension was considered as the first etiological disorder in 14 cases; syphilitic aortic insufficiency in 6, arteriosclerosis in 5; and rheumatic condition in 2. The two last mentioned had mitral stenosis and one of them also had aortic insufficiency.

The occurrence of nocturnal dyspnea is restricted almost entirely to patients with disorders which cause a strain on the left ventricle. Cardiac enlargement and diminished vital capacity were constant objective findings; premature beats and gallop rhythm occurred in a large number of the patients. Only 4 patients in the series had auricular fibrillation. Eight patients had angina pectoris, but only 4 of them had ever suffered the pain and the dyspnea simultaneously. Uncomplicated syphilitic aortitis (*i. e.*, without aortic insufficiency, occlusion of the coronary vessels or aneurism) practically never causes nocturnal dyspnea.

The authors subdivide nocturnal dyspnea into several types, as follows

"1 A type which is not paroxysmal, but which develops gradually during the course of the day, usually appearing first in the late afternoon and reaching its maximum intensity at bedtime. For this syndrome the name 'evening dyspnea' is proposed.

"2 Attacks of shortness of breath appearing only at the onset of sleep and tending to prevent the patient from reaching a state of deep sleep. However, if such a patient falls into a sound sleep, he is likely to remain free from attacks throughout the remainder of the night. Patients with this type of dyspnea frequently exhibit Cheyne-Stokes respiration and are unlikely to have seizures of acute pulmonary edema.

"3 Attacks of dyspnea which begin after the patient has begun to sleep soundly and which are likely to cause acute edema of the lungs. Cheyne-Stokes respiration is an infrequent finding in patients with this type of dyspnea.

"4. Combination forms. The same patient may have all 3 types of dyspnea, or any 2 of them."

Attacks of acute pulmonary edema were observed in 6 of the 30 patients. All these attacks appeared after the individual had been asleep for some time, and no attack occurred at the onset of sleep. Furthermore, no patient whose dyspneic seizures were limited in occurrence to the onset of sleep has had an attack of acute pulmonary edema. The average age of the 8 patients who had paroxysmal dyspnea only at the onset of sleep was 55 years, the youngest being 43, and the oldest, 68, whereas the average age of the 10 subjects suffering



attacks which awakened them from sound sleep was 42 years, the range being from 23 to 54 years.

### **ELECTROCARDIOGRAPHY.—BUNDLE-BRANCH BLOCK.—**

An analysis of 155 instances of bundle-branch block in 150 patients, made by J. T. King (Am J. M. Sc 187 149 (Feb ) 1934), at the Johns Hopkins Hospital, revealed arteriosclerotic heart disease as the background in 69.5 per cent of the cases, syphilis in 9 per cent, rheumatic infection in 9.7 per cent, while in 11.8 per cent. the etiologic agent was in doubt. Comparison showed that bundle-branch block might be expected to occur in only about 2 per cent of all patients suffering from syphilitic cardiovascular disease and in 5.5 per cent of all patients with rheumatic infection of various types, at least in the vicinity of Baltimore. The average age of patients with this abnormality associated with senile heart disease was 61 years, 4.3 months, of those with syphilitic heart disease 42 years, 3.3 months; of those with rheumatic heart disease 42 years, 4 months. Men constituted 73 per cent, and women 27 per cent of the patients in the series.

The number of cases of bundle-branch block at the Johns Hopkins Hospital increased sharply from the year 1917 to 1924, with no significant change thereafter. This increase is very likely the result of the increasing use of the galvanometer. While no social class is immune to branch block, it occurs most frequently among laborers, least frequently among housewives and those following professions, business men show an incidence to the condition in proportion to their number in the whole Hospital population. Previous infections appeared to play no specific part in etiology except in the rheumatic group, in which the history of tonsillitis and gummy was relatively high.

Prolongation of the P-R interval occurred in 28 cases of branch block (18 per cent), complete A-V dissociation occurred in 36, auricular fibrillation in 26, flutter in 3. Over a 5-year period (1927 to 1931, inclusive) in which 329 instances of auricular fibrillation were met with, there were found 78 cases of bundle-branch block, 28 of complete auriculoventricular dissociation, and 20 of auricular flutter.

Reduplication of the apex thrust—a quick repetition of the apex impulse—may be seen in 84 per cent and felt in 80 per cent of all cases of bundle branch block (J. T. King and D. McEachern. Am J. M. Sc 183 445 (Apr ) 1932). Various auscultatory phenomena encountered in bundle-branch block are recorded in diagrammatic form (Chart I).

The diagram is intended to convey merely impressions of audition, no attempt having been made at accurate timing of the various elements. The first sound is represented throughout as faint, except in the first line, where the sounds are shown as normal, this *muffling, or reduction in intensity, amounting, in some cases, virtually to inaudibility of the first sound*, is one of the most common and striking signs. However, even when the sound is inaudible, perhaps through the lift of the stethoscope, a sense of reduplication at the beginning of systole might be obtained: such a finding is represented on the fourth line. The shaded blocks which take the place of the second element of the first sound (as in Line 5) and



of both elements of the first sound (as in Line 6) represent murmurs in systole. The author emphasizes strongly that the auscultatory findings are of secondary importance to the visible and palpable reduplication of the systolic thrust in the bedside diagnosis of bundle-branch block. Where there is an apparent contradiction between the surface findings at the cardiac apex and the auscultatory signs, the auscultatory signs should be disregarded. However, as secondary, supporting indications, they are of some interest

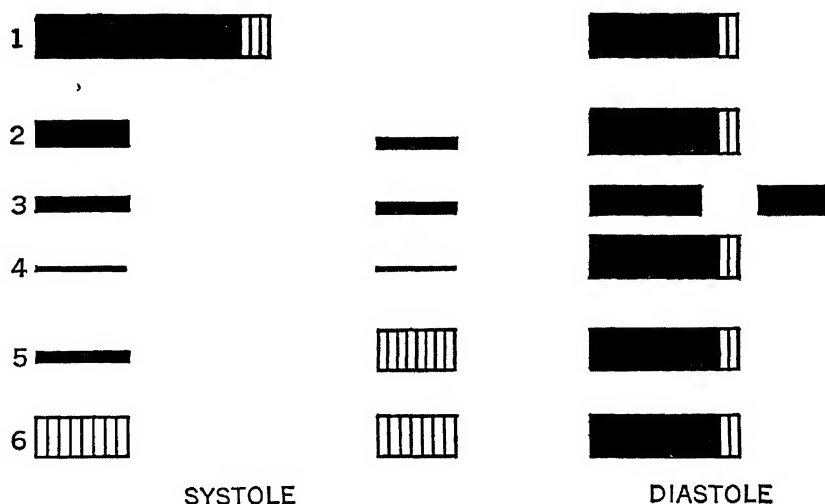


Chart I—A diagrammatic suggestion of auscultatory phenomena of bundle-branch block (1) Normal sounds—an occasional finding, (2) reduplication of  $S_1$  (common), (3) reduplication of  $S_1$  and  $S_2$ , (4) almost complete absence of  $S_1$ , (5) soft  $S_1$  with an asynchronous murmur, (6) asynchronous systolic murmurs (King and McEachern Am J M Sc)

In a previous communication, King (Am Heart J 3 505 (June) 1928) assumed that the reduplication of the first sound and the bifid apex thrust in bundle-branch block are associated with asynchronous movements of the ventricles. Previous experimental evidence had indicated that asynchronism of the ventricles follows section of one of the bundle branches. This view is substantially strengthened by the work of C. C. Wolferth, A. Margolis, and S. Bellet (Tr. A. Am. Physicians 48 187, 1933), who have produced evidence of asynchronism of the ventricles in bundle-branch block in the human being, and have also shown that the reduplication of the first sound appears during ventricular systole.

The prognosis in bundle-branch block is very grave, regardless of etiology, though it appears best in the rheumatic group. Since some patients live for a considerable period, perhaps its presence should be looked upon as an omen of very great import rather than as a necessarily fatal handicap. Of 104 patients who could be traced, 76 were reported dead. The average duration of life following diagnosis was 1 year for the senile group, 10.6 months for the syphilitic, and 1 year, 8 months for the rheumatic group. Of 28 patients reported to be alive, the average time between diagnosis and the report was 1 year and 9 months in the senile group; 1.5 months in the syphilitic; 2 years and 8 months in the rheumatic.

**CORONARY DISEASE.—Initial Ventricular Deflections.**—The observations of F. N. Wilson, A. G. MacLeod, P. S. Barker, F. D. Johnston and

L. L. Klostermeyer (Heart 16.155 (June) 1933) regarding changes in the initial deflections of the ventricular complex in *myocardial infarction* have been followed by studies by other investigators. Wilson and his associates found that characteristic changes in the R-S-T segment and T deflection of the electrocardiogram in coronary occlusion are very frequently accompanied by modifica-

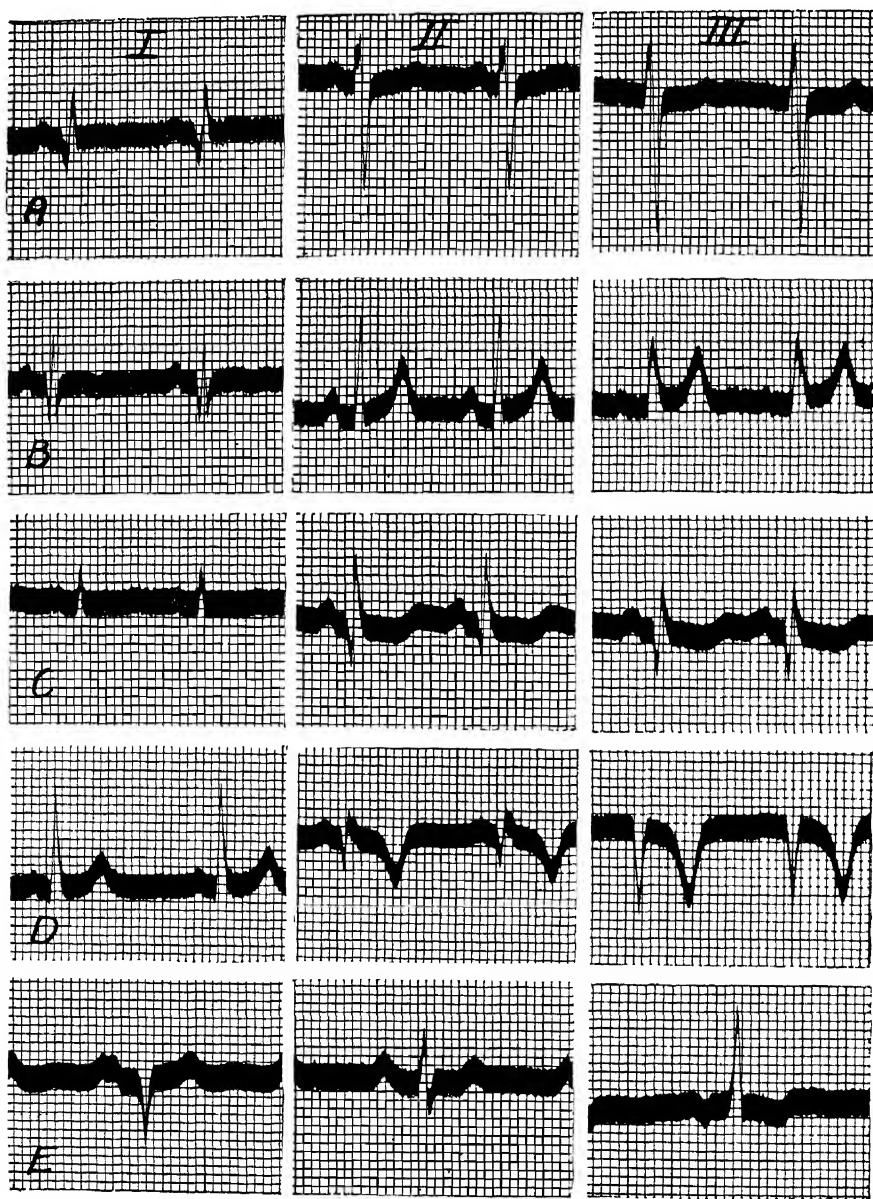


Fig 1—(A) and (B) Curves of the  $Q_1$  type, (C) and (D) curves of the  $Q_1$  type, (E) an electrocardiogram showing large  $Q$ -waves in Lead I. This curve is from a case of mitral stenosis (Durant: Am J M Sc)

tions of the initial ventricular deflections of a more or less distinctive kind, which they classified under the headings of  $Q_1$  and  $Q_3$  types. Curves of the  $Q_1$  type are characterized by a "conspicuous and, in most instances, rather broad  $Q$  in Lead I; the absence of  $Q$  in Leads II and III; the small amplitude of the largest of the initial deflections in Lead I; and the presence of a conspicuous  $S$  in Leads

II and III." The features most characteristic of the Q-R-S group in curves of the Q<sub>3</sub> type are "absence of Q in Lead I, the presence of a conspicuous Q in Leads II and III, and the relatively small amplitude of the initial ventricular deflections in Lead II."

In an effort to ascertain how frequently curves of the Q<sub>1</sub> and Q<sub>3</sub> types (Fig. 1) are encountered in individuals in which there is no other reason for suspecting coronary disease and to determine what criteria, if any, could be used to differentiate between the Q-R-S changes due to coronary disease and similar changes due to other causes, T. M. Durant (Am. J. M. Sc. 188:225 (Aug.) 1934) analyzed approximately 7000 electrocardiograms obtained from the files of the University Hospital, Ann Arbor, Michigan. All curves with abnormal Q-R-S deflections of the kinds in question were carefully studied.

*Electrocardiograms of Q<sub>3</sub> Type*—It was soon found advisable to omit one of Pardee's\* requirements, viz., that Q<sub>3</sub> be followed by a summit (R), but no S deflection. This change resulted from the discovery that a number of cases of definite coronary occlusion with large Q-waves in Lead III failed to conform to this standard. Fig 1, D, the electrocardiogram from a case of coronary occlusion proved by autopsy illustrates this point. For similar reasons it was found unnecessary to eliminate curves with slight notching of the down-stroke of Q<sub>3</sub> (the W complex of Pardee). Curves showing right axis deviation were excluded. There were 96 electrocardiograms which met these qualifications, and a study of their histories revealed 31 cases of coronary occlusion and 29 cases of angina pectoris (Table I, A).

TABLE I  
Q<sub>3</sub> GROUP.

Criteria	Total Cases	Coronary Disease			No Evident Coronary Disease	Percentage Coronary Disease
		Coronary Occlusion	Angina pectoris	Total		
A Q <sub>3</sub> at least 25% of largest Q-R-S deflection Q <sub>2</sub> at least 1 mm Left axis deviation or normal axis	96	31	29	60	36	62.5
B Q <sub>3</sub> at least 50% of largest Q-R-S deflection Q <sub>2</sub> at least 25% of R <sub>2</sub> Left axis deviation or normal axis	44	25	11	36	8	81.8
C Same as under B, and in addition T-wave inversion in Leads II and III, but not in Lead I	22	18	4	22	0	100.0

\* That large Q-waves in Lead III occur very frequently in association with the anginal syndrome was first pointed out by H. E. B. Pardee (Arch. Int. Med. 46:470 (Sept.) 1930). He concluded that the presence of a Q-wave in Lead III was of diagnostic value when it was followed by an upward excursion (R) but no S-wave, and is at least one-fourth as large as the largest Q-R-S deflection in any lead. No significance was attached to large Q-waves in Lead III when definite right axis deviation was present or when the initial deflection in Lead III resembled the letter M or the letter W in shape. In a group of electrocardiograms meeting these qualifications, 63 per cent were found to be associated with the anginal syndrome.

The remaining patients gave no history and showed no physical signs suggesting anginal pain or coronary occlusion.

With the thought that more satisfactory results might be obtained by further modifications of the criteria, the requirements finally selected were as follows: (1) an initial downward deflection in Lead III having an amplitude at least one-half as great as the Q-R-S deflection in any lead, (2) an initial downward deflection in Lead II at least one-fourth as large as  $R_2$ , and (3) left axis deviation or a normal electrical axis. Of the 44 cases which conformed to these standards, 81.8 per cent presented clear evidence of angina pectoris or coronary occlusion (Table I, B). Of the 8 patients without coronary disease, 4 had generalized arteriosclerosis and 1 arteriosclerotic heart disease. The other 3 patients, with no evident coronary disease, included 2 with adenomatous goiter, 1 of whom showed definite hyperthyroidism, and the third suffered with obesity and cholecystitis, without any demonstrable cardiac disease.

By adding to the requirements, T-wave inversion in Leads II and III without inversion in Lead I, the number of cases was reduced to 22, all of whom were clear-cut examples of coronary disease (Table I, C). Therefore, when both Q-R-S changes and T-wave changes of the type under consideration are found, the presence of coronary disease is practically certain. However, in the absence of changes in the final deflections, a fairly high degree of diagnostic accuracy is obtained from the Q-R-S variations alone.

*Electrocardiograms of  $Q_1$  Type*—At first, tracings with the following characteristics were selected: A Q-wave in Lead I, measuring at least 1 mm and at least one-fifth as large as the largest R in any lead, and an  $R_1$ , not exceeding 5 mm in height. The incidence of coronary disease in this group of cases (Table II, A)

TABLE II  
 $Q_1$  GROUP

Criteria	Total Cases	Coronary Disease			No Evident Coronary Disease	Percentage Coronary Disease
		Coronary Occlusion	Angina Pectoris	Total		
A $Q_1$ at least 1 mm $R_1$ less than 5 mm $Q_1$ at least 20% of largest R.	32	13	4	17	15	53.1
B Same as under A, and in addition curves eliminated in which no $R_1$ is present	23	13	4	17	6	73.9
C Same as under B and, in addition, inversion of $T_1$ , without inversion of $T_2$ or $T_3$	14	10	3	13	1	92.8

was relatively low because of the inclusion of a number of cases of mitral stenosis. Most of these and a few others in which there was no evident coronary disease were eliminated when all tracings that failed to show a summit (R) following  $Q_1$  were excluded. In Fig 1, E, is shown a tracing from a case of mitral stenosis thus eliminated. The 6 cases without evident coronary disease that were not

eliminated were classified as follows: Mitral stenosis 2, congenital heart disease 1, arteriosclerotic heart disease with congestive failure 2, exophthalmic goiter 1.

The addition of changes in the final ventricular deflection of the  $T_1$  type raised the incidence of coronary disease to 92.8 per cent (Table II, C). One case of congenital heart disease showed both Q-R-S and T-wave changes and could not be excluded.

The diagnostic value of electrocardiographic changes of the  $Q_1$  type is considerably enhanced by the fact that the cases most often causing confusion, *viz.*, mitral stenosis and congenital heart disease, are, as a rule, readily eliminated by the clinical findings. Disregarding the 2 cases of mitral stenosis and 1 case of congenital heart disease, the incidence of coronary disease under II, B becomes 85 per cent, a figure comparable to that obtained for curves of the  $Q_3$  type.

Of 74 cases in which the diagnosis of coronary occlusion was certain, 13 satisfied the criteria given in Table II, B; and 25 curves were of the  $Q_3$  type and met the requirements given in Table 1, B. Hence, 38 cases (51.3 per cent. of the total number) showed initial ventricular deflections of either the  $Q_1$  or the  $Q_3$  type. The author concludes, therefore, that initial ventricular variations of the kinds described are infrequent in conditions other than coronary disease, occurring in approximately one-half of the cases of coronary thrombosis, and that any modification of the diagnostic criteria which tends to eliminate noncoronary cases, also excludes some cases of coronary disease.

M. Winternitz (Am Heart J 9:616 (June) 1934) has reported 15 cases of his own and has cited 26 cases from the literature in which characteristic changes appeared in the initial complex following a coronary closure. The changes, which

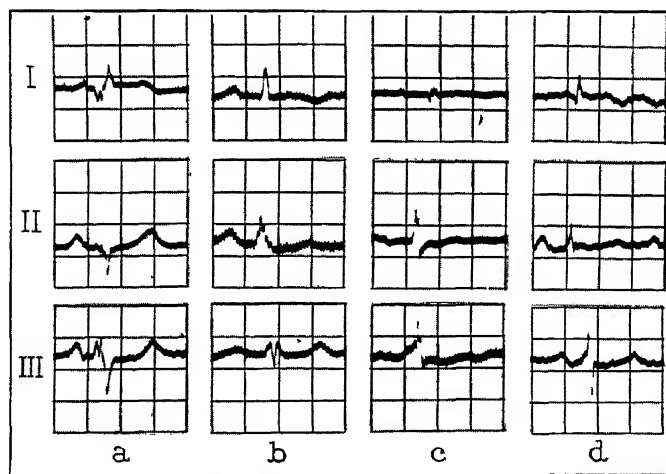


Fig. 2—Four different patients. (a) Electrocardiogram taken 2 days after acute coronary occlusion. Typical  $Q_1$  and  $T_1$  type. Necropsy disclosed acute and chronic infarction of the anterior and apical portion of the left ventricle. (b) Electrocardiogram taken 24 hours after the onset of an attack of acute coronary occlusion. A fairly typical  $T_1$  but no Q pattern is present. Necropsy was not performed. (c) Electrocardiogram taken 12 weeks after an attack of acute coronary occlusion. The  $Q_1$  type of change is definitely present and strongly supports the diagnosis of myocardial infarction. No R-T pattern can be recognized, probably because of the extreme low amplitude of all deflections in Lead I. (d) Electrocardiogram taken 2 years after a typical attack of acute coronary occlusion. Necropsy disclosed ancient and recent infarction in the apex of the left ventricle. No history of recent acute occlusion was obtained. The  $T_1$  pattern is probably present, but it is difficult to be sure of the characteristics of the R-T segment in Lead I. The presence of a fairly well developed  $Q_1$  pattern greatly strengthened the diagnosis of myocardial infarction.

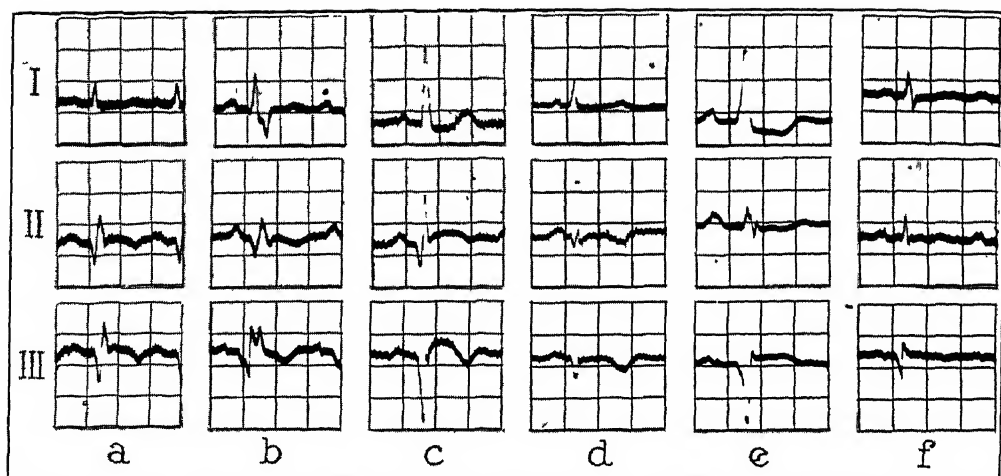


Fig 3—Five different patients. (a) Electrocardiogram taken 4 months after an attack of acute coronary occlusion. The contour of the R-T segment in Lead III and the slight inversion of the T-wave in Lead II are slightly suggestive of ancient acute cardiac infarction. The presence of a typical  $Q_1$  type of change in the initial deflections tremendously strengthens the diagnosis. (b) Electrocardiogram taken after acute myocardial infarction. The time of coronary occlusion could not be obtained because the patient was in coma. There is a definite suggestion of a  $T_1$  type of change. There is a typical  $Q_1$ , but no definite  $Q_2$  deflection present. Necropsy disclosed acute infarction of the basal posterior half of the left ventricle. (c) Electrocardiogram taken 2 weeks after an attack of acute coronary occlusion. A fairly typical late  $T_1$  pattern of acute myocardial infarction is present, but a  $Q_1$  pattern has not developed. (d) Electrocardiogram taken 2 years and 8 months after acute coronary occlusion. The electrocardiogram obtained at the time of occlusion showed a typical  $T_1$  type of change. The present electrocardiogram has, as a relic of that event, an R-T segment in Lead III of the  $T_1$  type. However, that change alone does not carry conviction of previous acute cardiac infarction. The  $Q_1$  pattern is typically developed except for the absence of  $Q_2$ . The two patterns taken together constitute strong evidence of previous acute myocardial infarction. (e) Electrocardiogram taken 1 week after acute coronary occlusion. The  $T_1$  pattern is typically developed. The  $Q_1$  pattern is atypical in that the initial deflection has its lowest amplitude in Lead I rather than in Lead II. (f) Tracing taken on the same patient as the one represented in (e). 39 months later. The Q and T patterns have retained their original characteristics in about equal degree.

appeared immediately or some time after the *occlusion*, and remained definite or regressed, are classified in 3 groups. The characteristics of *Group 1* are a modified form of left axis deviation with small R-wave in Lead I, with  $S_1$  absent or rudimentary and  $Q_1$  present or absent, while Leads II and III are dominated by a deep S-wave, greater than any of the other waves of any lead. In the *second group*, negativity of the principal deflection of all leads is the chief characteristic, whether this be S or Q, usually, too, the waves are smaller than normal. The *third group* is characterized by the shrinking of all the main waves, while smaller deflections may persist unchanged. The anatomical basis for the first two groups is an extensive necrosis of the anterior wall of the heart; for the third group it is necrosis of the anterior and posterior walls as a result of two thromboses. Through a control study of 1460 electrocardiograms, chosen at random, these changes were found to be not pathognomonic, but most suggestive of the presence of infarct of the heart. They occur less frequently than do the heretofore recognized signs of coronary thrombosis, but they may be present in those cases in which there are no characteristic changes in the final complex. Attention is called to the fact that the electrocardiographic change discussed by Winternitz bears many of the characteristics of the "curves of the  $Q_1$  type" described by Wilson and his associates.

**Q and T Types of Electrocardiograms.**—In a review of 84 electrocardiograms of patients who had suffered from attacks of acute myocardial infarction,

A. R. Barnes (Am Heart. J. 9:722 (Aug) 1934) points out that a combined study of the Q and R-S-T patterns frequently yields more information than either pattern alone. When a diagnosis of myocardial infarction was based only on *clinical evidence*, the Q and T patterns were equally characteristic in 18 cases; the Q<sub>1</sub> pattern (see Fig. 2) more characteristic than the T<sub>1</sub> pattern in 6; the T<sub>1</sub> more typical than the Q<sub>1</sub> type in 10; the Q<sub>3</sub> (see Fig. 3) more suggestive of acute infarction than the T<sub>3</sub> type in 6; the T<sub>3</sub> more diagnostic than the Q<sub>3</sub> in 15; the Q<sub>1</sub> pattern of infarction was present in the absence of the T<sub>1</sub> pattern in 1; the T<sub>1</sub> pattern was present alone in 3; the Q<sub>3</sub> pattern occurred alone in none, and in 2 cases, the T<sub>3</sub> pattern was present in the absence of the Q<sub>3</sub> pattern.

When myocardial infarction was proved at *necropsy*, the Q and T patterns were equally positive in 11 cases; the Q<sub>1</sub> type was more typical than the T<sub>1</sub> type in 3; the T<sub>1</sub> type was more characteristic than the Q<sub>1</sub> type in 1; the Q<sub>3</sub> pattern was more suggestive than the T<sub>3</sub> type in 4, and the T<sub>3</sub> pattern offered more evidence of cardiac infarction than the Q<sub>3</sub> in 3.

"There are several circumstances that account for the failure of the Q and T types to occur with equal clearness at a given time. In anterior apical infarction, the initial deflection of the electrocardiogram may have a very low amplitude. This so reduces the height of the R-T segment displacement that the change in level and contour of the segment and the inversion of the T-wave are all but unrecognizable. Under these conditions the Q<sub>1</sub> pattern may be present and easily recognizable. Likewise, in infarction in the posterior basal portion of the left ventricle, the amplitude of the initial ventricular deflection in Lead II may be small. On this account, changes in the level and contour of the R-T segment in this lead characteristic of a T<sub>3</sub> type may be difficult to recognize, and the presence of a Q<sub>3</sub> pattern may be of crucial importance. In certain instances, infarction in the anterior apical portion of the left ventricle is followed by nothing more than slight rounding and upward displacement of the R-S segment in Lead I, without a corresponding depression of the S-T segment in Lead III. In this instance, the occurrence of a Q<sub>1</sub> pattern greatly strengthens the evidence of infarction.

"Either the Q or T patterns may become positive first following acute infarction. They may remain as a relic of infarction equally long. However, in some instances, the Q pattern may retain its identity longer than the T pattern, as Wilson pointed out. In tracings under consideration at the clinic, this occurred occasionally, with the T<sub>3</sub> type of electrocardiogram at a stage when the R-T changes in Lead II had returned to normal.

"Acute pericarditis complicating acute myocardial infarction frequently produces an anomalous type of electrocardiogram. This complication is prone to be followed by elevation of the R-S-T segment in all leads, a picture which cannot be classed definitely as a T<sub>1</sub> or T<sub>3</sub> type of change. This situation may be greatly clarified if a definite Q pattern develops simultaneously.

"The Q types of change may be confusing, and actually portions of Q<sub>1</sub> and Q<sub>3</sub> patterns may exist simultaneously in cases in which successive occlusions have occurred. The relic of a Q pattern from a healed acute infarction may persist in some degree following a second infarction, leading to the development of a Q pattern approximating the opposite type. Here the T type of electrocardiogram may give more nearly unequivocal evidence of acute myocardial infarction than does the Q pattern.

"And, finally, acute myocardial infarction is followed at times by the development in the electrocardiogram of typical T patterns without the appearance of Q types of changes."

In a study of 20 autopsied cases in which myocardial infarction occurred and in which electrocardiograms conformed more or less closely to the Q<sub>1</sub> or Q<sub>3</sub> types, A. R. Barnes (*Ibid.* p 728) has correlated the initial deflections of the

ventricular complex with the situation of the infarction. In 7 cases with electrocardiograms, typical or fairly typical  $Q_1$  types, infarction was found in the anterior portion of the left ventricle and the adjacent septum. In each of these instances the  $Q_1$  type of electrocardiogram was associated with changes in the tracing conforming more or less closely to the  $T_1$  type. In 15 cases with a  $Q_3$  type of electrocardiogram, infarction was found in the posterior basal portion of the left ventricle. In each of these cases the  $Q_3$  and  $T_3$  types of change were present simultaneously.

A strong argument in favor of the existence of a uniform relationship between the  $Q$  pattern and the situation of infarction was afforded by 2 patients, each of whom suffered 2 successive acute infarctions. A time interval permitted adequate electrocardiographic studies after each infarction. In 1 case, acute infarction in the anterior portion of the left ventricle was followed by the development of  $Q_1$   $T_1$  type of electrocardiogram, and a second acute infarction in the posterior basal portion of the left ventricle caused a complete change of pattern to a late  $T_3$  type and a picture approaching a  $Q_3$  type. That a typical  $Q_3$  type was not reached may possibly be owing to the necessity for completely obliterating the previous  $Q_1$  type. In the second case the order of these changes was completely reversed.

The author has never encountered a case with a typical  $T_1$  type of electrocardiogram in which a typical  $Q_3$  pattern occurred and he has observed no association of typical  $T_3$  and  $Q_1$  patterns. When anterior infarction succeeds posterior infarctions an atypical  $Q_3$  pattern may remain in association with a  $T_1$  type of electrocardiogram, but the  $Q_3$  pattern is atypical, and careful study will show that it is veering definitely toward a  $Q_1$  pattern. Extremely low voltage of the initial ventricular deflections, bundle-branch block, multiple acute infarcts involving both the anterior and the posterior portions of the left ventricle, massive wide-spread infarction, acute pericarditis or the effect of imminent death on a tracing may modify, obscure, or prevent the recognition of either the  $T$  or the  $Q$  pattern. Furthermore, the electrocardiographic picture of acute myocardial infarction may be lost if electrocardiograms are not taken in sufficient number, or in proper relation to acute coronary occlusion. As pointed out by Wilson and his associates, the pathological data and experimental evidence to date do not seem sufficient to attribute the development of the  $Q_1$  type of electrocardiogram to block in the anterior subdivisions of the left branch of the bundle of His, nor to ascribe the  $Q_3$  type to block in the posterior subdivisions of the bundle of His.

According to Barnes (*Ibid*, p. 734), the electrocardiograms of patients with acute coronary occlusion complicated by *pericarditis* differ from the type of R-S-T changes associated with uncomplicated, acute coronary occlusion. The typical feature of the electrocardiogram in coronary occlusion associated with pericarditis in its early stages consists of elevation or upward rounding of the R-S-T segment in all leads. This may be followed by inversion of the T-wave in all leads. In some instances, it is followed by the development of a T pattern that can be classified definitely as a late relic of acute coronary occlusion. In the stage when the R-S-T segment is elevated in all leads, the  $Q$  pattern may be typically developed, not only indicating infarction, but also pointing to the situation of the infarct in the left ventricle.



**Large Q-wave in Lead III of Electrocardiogram.**—In an analysis of 103 electrocardiograms with a significant Q-wave in Lead III, by R. France (Am J M Sc 187 16 (Jan.) 1934), the anginal syndrome was found in 46 (45 per cent); hypertension without the anginal syndrome in 19 (18 per cent); and chronic, nonvalvular heart disease without hypertension or anginal syndrome in 16 (16 per cent.). Angina pectoris was suffered by 23 (72 per cent.) of 32 patients whose records showed, in addition to a large Q<sub>3</sub>, one or more of the fol-

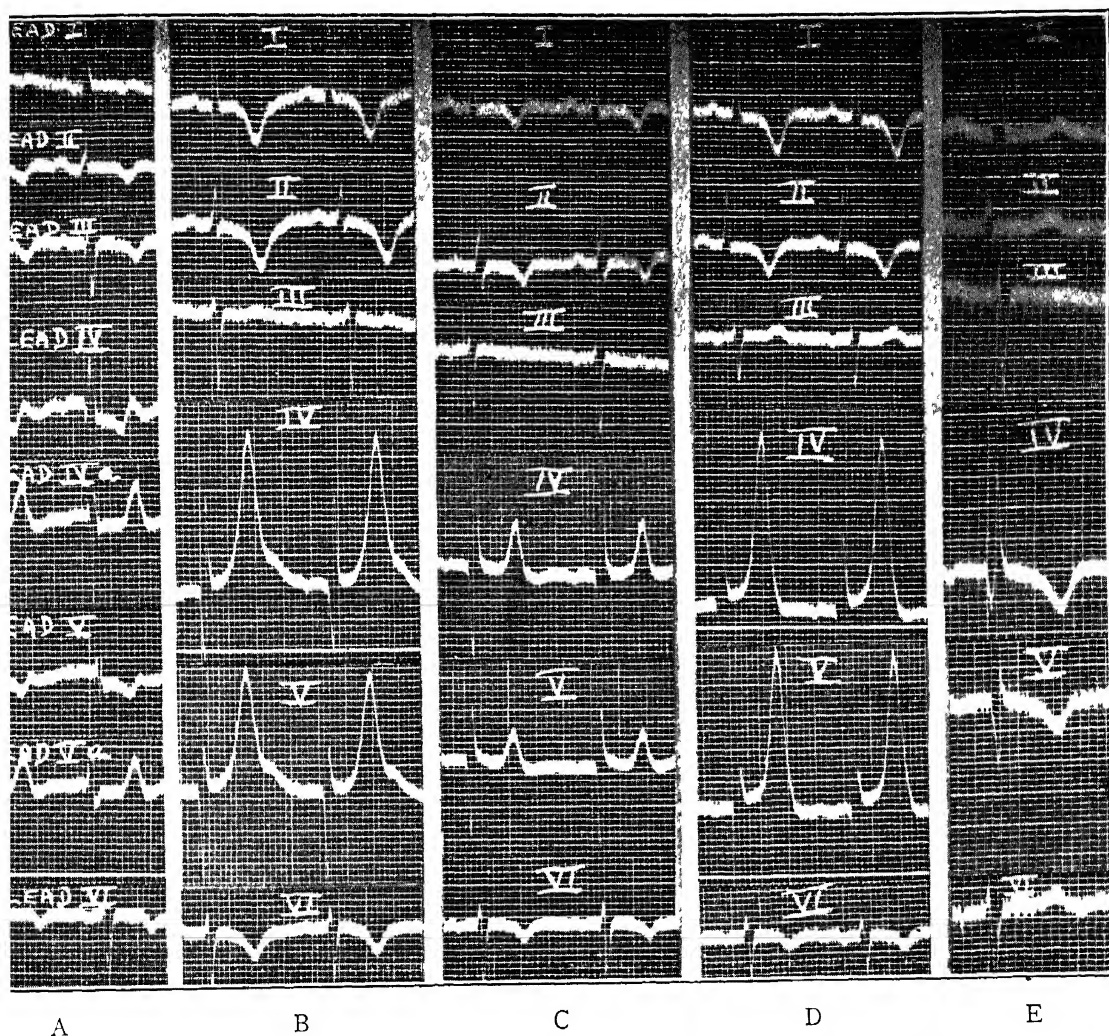


Fig 4—Electrocardiograms of Case 4. Patient had attack of cardiac pain on March 11, 1933. All tracings in this figure, except when otherwise stated, were taken with the anterior chest electrode at apex impulse. The largest T-waves were obtained from a point 3 cm to left of apex.

(A) Tracing taken March 11. Lead I shows a slight RS-T interval elevation. Lead II shows an inverted T-wave. Lead IV shows a small initial downward deflection of QRS, a slight depression of the RS-T interval, and a diphasic T-wave. Lead V shows an M-shaped QRS complex. Leads IV<sub>a</sub> and V<sub>a</sub> were taken with anterior electrode 4 cm. to left of apex impulse. They show marked differences from Leads IV and V, which were taken from apex.

(B) Tracing taken March 13. Large inverted T-waves have appeared in Leads I and II. Huge upright T-waves are present in Leads IV and V, 24 mm and 18 mm high. T<sub>a</sub> has become quite deeply inverted. RS-T interval in Leads IV and V slightly elevated.

(C) Tracing taken March 20. All T-waves are smaller.

(D) Tracing taken April 10. All T-waves have become large once more, resembling those on March 13. By May 16 the T-wave had again become quite small.

(E) Tracing taken January 6, 1934. Left axis deviation is only abnormality which has persisted.

lowing changes: (1) inversion of (a)  $T_1$  or (b)  $T_2$  and  $T_3$ ; (2) high or low takeoff of the R-S-T interval in Leads I or III; (3) slurring at the apex of  $R_1$  or  $S_1$ . Findings in the 12 patients who came to autopsy support the view that occlusion of the right coronary artery with subsequent infarction of the posterior base of the left ventricle and available portion of the interventricular septum constitutes an important factor in the production of a large Q-wave in Lead III.

**Huge T-waves in Precordial Leads in Cardiac Infarction.**—F. C. Wood and C. C. Wolferth (Am Heart J. 9:706 (Aug.) 1934) call attention to the significance of huge T-waves in the precordial leads of the electrocardiograms in acute coronary occlusion. Of 7 cases reported, 6 showed huge, upright T-waves in Leads IV or V, which exceeded 13 mm. in amplitude (Fig. 4), and 2 had an *inverted* T-wave, 19 mm. deep, in Lead V. In each instance, the electrocardiographic string deflection was standardized carefully and skin resistance was kept low, so that no "overshooting" occurred. These huge, upright T-waves present an appearance distinctly different from anything seen in a series of 550 controls. Fairly large upright T-waves often do appear in precordial leads during the healing of an anterior cardiac infarct, however, among a group of 78 patients with acute coronary occlusion, studied with chest leads by the authors, the 6 cases reported in this study are the only ones in which the T-wave in Lead IV or V exceeded 10 mm. in height. These bizarre waves may appear on the day of the attack or not until days or weeks later, also, their time of disappearance may vary considerably. They are sometimes elicited from a small area of the precordium only, and, if the anterior electrode is placed elsewhere on the anterior chest wall, they may not appear in the tracing. R-S-T interval deviations may be absent in these cases.

Although the patients in this group presented the clinical picture of coronary occlusion, the symptoms and signs immediately associated with the huge T-waves tended to be less severe than the classical text-book description of the disease. A rather striking feature was the liability to frequent recurrences of cardiac pain for days or even weeks after the onset. The mildness of the symptoms suggests that the lesion is either complete occlusion of a small coronary vessel or partial occlusion of a large one.

With one exception, all the cases with huge upright T-waves in Leads IV or V presented electrocardiographic features more or less indicative of infarction in the anterior surface of the left ventricle. The one case which came to autopsy showed a large infarct in the anterior surface of the left ventricle. Very large inverted T-waves in precordial leads probably signify a lesion in the posterior surface of the left ventricle, analogous to that causing high upright T-waves.

**Electrocardiogram of Low Voltage.**—Coronary arteriosclerosis of significant degree was found in 76 per cent. of 50 cases with electrocardiograms of low voltage (the maximum excursion not exceeding 7 mm.) reported by L. G. Steuer (Am. Heart J. 9:405 (Feb.) 1934). The patients were from the wards of the Cleveland City Hospital, and all came to autopsy. In 21 cases (42 per cent.) there was coronary sclerosis of moderate degree to complete occlusion with frequent thrombus formation; in 17 cases (34 per cent.) there was a significant degree of coronary sclerosis, but the latter finding could not be considered the

primary lesion; and in the remaining 12 cases (24 per cent.) acute and chronic infections of various types played the predominating rôle. Of particular interest were 2 cases of cancer which presented no evidence of cardiac disease except such as might accompany cachexia

**Coronary T-wave in Pericarditis.**—A A F. Peel (Glasgow Med. J. 4 137 (Oct) 1934) reports 6 cases in which pericarditis was associated with displacement of the R-T segment similar to that which occurs in coronary thrombosis. Of 48 cases of pericarditis, some abnormality of the R-T or T segment was found in 29 (60 per cent), though in only 17 (35 per cent) could other possible causes be excluded. In 19 (40 per cent) the R-T and T segments were normal, though in one-third of them other electrocardiographic evidence of myocarditis was obtained. The evidence points to myocarditis rather than pericardial effusion as the cause of the R-T and T-wave changes, although experimental work in the literature shows that they can be produced by raising the intrapericardial pressure. In a proportion of cases, though not in all, pericardial effusion caused diminished voltage of Q-R-S.

**LOW T-WAVES IN ELECTROCARDIOGRAM.**—In an extensive study of the significance of low T-waves in the electrocardiogram, made by J. Edeiken and C C Wolferth (Am J M Sc 187 778 (June) 1934), the clinical material consisted of the following groups: (1) 709 college students with presumably normal cardiovascular systems, (2) 23 cases having a "vertical" heart; (3) 25 pregnant women; (4) 202 cases showing a low T-wave (less than 2 mm) in Lead I or II or both, (5) 100 cases with normal electrocardiograms, (6) 143 cases with hypertension, (7) 145 railroad executives. T-waves less than 2 mm in amplitude in Leads I and/or II, and an R-1 of 6 mm amplitude or less were considered as low. The electrocardiograms were classified as follows: (A) Low T-wave in Lead I and normal T-wave in Lead II; (B) low T-waves in Leads I and II and either low or slightly inverted T-wave in Lead III; (C) normal T-wave in Lead I, low or flat T-wave in Lead II, and inverted T-wave in Lead III.

*Group I* In the records of 709 normal college students, there were found 34 cases which conformed to Type A (low T-wave in Lead I and normal T-wave in Lead II), 7 to Type B (low T-waves in Leads I and II and either low or slightly inverted T-wave in Lead III); and 5 to type C (normal T-wave in Lead I, low or flat T-wave in Lead II and inverted T-wave in Lead III). Analysis of the records showing a low  $T_1$  suggested a relationship between this wave and the Q-R-S complex of Lead I. In 32 cases the amplitude of the Q-R-S complexes was 6 mm or less and in 23, 4 mm or less. It seemed, therefore, that in young individuals with apparently normal hearts, a low T-wave in Lead I is encountered in less than 5 per cent of the cases and in most of these the Q-R-S complex is also of low amplitude. However, the converse is not true, for T-waves of normal amplitude are frequently found associated in Lead I with low Q-R-S complexes.

*Group II* In order to obtain some idea regarding the frequency of low  $T_1$  waves in cases with vertical hearts, a group of orthodiagrams exhibiting such hearts was selected. Only those orthodiagrams exhibiting a normal-sized heart

were chosen, records suggesting a "neutralized" heart were not included, and cases with evident cardiovascular disease were excluded. Twenty-three cases remained, and in 17 the R-waves in Lead I were 6 mm or less in amplitude; in 7,  $T_1$  was less than 2 mm. A low  $T_1$  was associated with a low  $R_1$  in 6 cases. Therefore, it would appear that in individuals with vertical hearts, a low Q-R-S complex is obtained in the majority in Lead I. Furthermore, the low Q-R-S complex frequently has associated with it a low  $T_1$ .

*Group III.* To study the influence of a high diaphragm upon  $T_3$ , the electrocardiograms of 25 pregnant women (ninth month) were examined. In 22,  $T_3$  was inverted, in 2 it was flat and in only 1 was it upright. Although factors other than a high diaphragm may influence the form of the electrocardiogram during pregnancy, it was noteworthy that in 10 cases examined after delivery,  $T_3$  which had been inverted became upright or flat in 9 and in only 1 there was no change. Although the T-wave in Lead III was of low amplitude in only 3 of the 25 cases, in each of these 3 cases  $T_1$  was inverted, following delivery,  $T_2$  became of normal amplitude and  $T_3$  upright. In all cases the T-wave in Lead I was of normal amplitude and in 13 cases 4 mm or more. Of the 10 cases examined after delivery, 9 showed a reduction in amplitude of  $T_1$ , although this reduction was slight in some cases, in 4 instances it was 2 mm or more.

*Group II\*.* In order to correlate the clinical and electrocardiographic findings in cases whose electrocardiograms showed a low T-wave in 1 or more leads, the records of 202 clinic and ward patients were studied. Of 68 cases which conformed to *Type A* (low T-wave in Lead I and normal T-wave in Lead II), the clinical records of 57 (83.8 per cent) showed cardiovascular abnormalities, 3 cases (4.4 per cent) were considered doubtful because their complaints or findings pointed to cardiac damage but sufficient evidence was not found to warrant a definite diagnosis, in 8 (11.8 per cent) there was no evidence of cardiovascular abnormality. Although 22 tracings showed a low  $R_1$ , in 5 cases there was mitral stenosis and right axis deviation, in 2, mitral stenosis without right axis deviation. In only 2 instances was there a vertical heart without evidence of organic disease. All of the remaining 13 cases showed some cardiac abnormality. Therefore, the association of low  $T_1$  and  $R_1$ , as found in Groups I and IV, may be due either to vertical position of the heart or to myocardial change, the incidence of each depending on the type of clinical material being studied. The *clinical diagnoses* of the 57 cases with cardiovascular abnormality were as follows: Hypertension and/or arteriosclerosis (including 3 cases of angina pectoris), 23; rheumatic heart disease, 10; myocardial disease (etiology unknown), 7; thyrotoxicosis, 6; syphilitic heart disease, 5; miscellaneous\*, 6.

Of 80 cases which conformed to *Type B* low T-waves in Leads I and II and either low or slightly inverted T-wave in Lead III, the clinical records of 70 (87.5 per cent) showed cardiovascular abnormalities, in 2 (2.5 per cent) the diagnosis was doubtful, and 8 (10 per cent) were negative. The *clinical diagnoses* of the 70 positive cases were: Hypertension and/or arteriosclerosis (including 2 cases of angina pectoris), 24; rheumatic heart disease, 12; myocardial

\* Such conditions as congenital heart disease, acute and subacute bacterial endocarditis, acute pericarditis, pleuropericarditis, metastatic carcinoma and severe cases of kyphoscoliosis.

disease (etiology unknown), 14; thyrotoxicosis, 10; syphilitic heart disease, 5; miscellaneous, 5.

Of the 54 cases which conformed to *Type C* (normal T-wave in Lead I, low or flat T-wave in Lead II and inverted T-wave in Lead III), 34 (63 per cent) showed cardiovascular abnormalities, 2 (3.7 per cent.) were doubtful, and 18 (33.3 per cent.) were negative. The *clinical diagnoses* of the 34 cases considered positive were: Hypertension and/or arteriosclerosis, 13; rheumatic heart disease, 6; myocardial disease (etiology unknown), 3; thyrotoxicosis, 5; syphilitic heart disease, 4; miscellaneous, 3.

*Group V* The clinical histories of 100 ward and clinic patients whose electrocardiograms were considered normal were studied as a control group. Of these, 41 were considered as having positive evidence of cardiovascular abnormality, 9 were doubtful, and 50 were considered negative. The *clinical diagnoses* of the 41 cases considered positive were: Hypertension and/or arteriosclerosis (including 1 case of angina pectoris), 16; rheumatic heart disease, 12; myocardial disease (etiology unknown), 1; thyrotoxicosis, 4; syphilitic heart disease, 5; miscellaneous, 3. The negative group consisted of a great variety of conditions. Although the patients in this group were derived from the same sources as those of Group IV, the different incidence of cardiovascular disease was striking, which fact points strongly to the significance of low T-waves.

*Group VI* In the group of 145 corporation executives, all of whom were active at the time of examination, there were 20 records with a *low T-wave in Lead I*. Clinically, 10 were considered as having a cardiovascular abnormality. Of the remainder, the low T-wave was associated with a low R in 7 instances; in 5 of these 7, the heart was vertical, and in 3 of the 5, it was smaller than normal. Of the 3 remaining cases, focal infection (teeth and tonsils) was stressed in the clinical records of 2, the third was considered negative.

Four records showed a *low T<sub>1</sub> and T<sub>2</sub>*. The electrocardiogram of one, a man of 32, showed a low R<sub>1</sub>, but clinically nothing was found but a few abscessed teeth. The other 3 presented findings indicative of cardiovascular disease.

Two cases had a *low T<sub>2</sub> and inverted T<sub>3</sub>*. One showed a slight increase in the width of the aorta on fluoroscopic examination but was otherwise negative, and nothing of significance was found on examination of the other.

*Group VII* Because of the large number of cases of hypertension showing a low T-wave in important leads (Group IV), a group of 143 cases of hypertension were studied. Only patients with systolic blood-pressure consistently above 150 mm or a diastolic pressure consistently over 100 mm were included. Left axis deviation was found in 95 (66.4 per cent), in 59 cases (41.3 per cent) the T-wave was diphasic or inverted in Leads I or II or both. In 30 instances (21 per cent) the T-waves corresponded to one of the types under consideration in the study, 15 to Type A, 12 to Type B, and 3 to Type C. The much greater incidence of these types in hypertension than in normal controls is evidence of their significance. Also, of interest is the fact that only 3 of the group of 30 cases with low T-waves showed a low R<sub>1</sub>.

Edeiken and Wolferth present the following conclusions:

"(A) An electrocardiogram with a low  $R_1$  and low  $T_1$  and a normal  $T_2$  points either to abnormality of the heart or to vertical position. When the heart is vertically placed, no significance can be ascribed to these findings as evidence of cardiac abnormality. When, however, the heart occupies its usual position, the low  $R_1$  and  $T_1$  suggest that it may be abnormal.

"(B) The association of a normal or high  $R_1$  and a low  $T_1$  offers strong but not certain evidence of cardiac abnormality.

"(C) The finding of small T-waves in all leads is probably rarely, if ever, dependent on position of the heart. It furnishes strong presumptive evidence of abnormality of the heart.

"(D) The combination of a normal  $T_1$ , a low or flat  $T_2$  and an inverted  $T_3$  may be due either to abnormality of the heart or to a more transverse position than is usual. When the heart is transversely placed, such an electrocardiogram may not be regarded as evidence of myocardial abnormality, when, however, the heart occupies the usual position, such a tracing suggests myocardial abnormality.

"(E) It is possible that in a small minority of cases, these various types of electrocardiograms may occur in the absence both of altered position of the heart and abnormality of the myocardium."

**CHANGES IN S-T SEGMENT OF ELECTROCARDIOGRAM IN ACUTE RHEUMATIC FEVER.**—In a review of the literature and a report of 3 personal cases, M. H. Easby, and H. Roesler (Ann Int Med 8:46 (July) 1934) call attention to the changes in the electrocardiogram in acute rheumatic fever. Prolongation of the auriculoventricular conduction time and alterations of rhythm are the changes best known, however, S-T changes are not uncommon. In their 3 cases the following electrocardiographic changes were observed: (1) S-T (R-T) segment with a low or high takeoff, a convex upward bowing, a depression, or an absence of the isoelectric portion, (2) T-wave showing isoelectricity, low voltage, origin below the basal line, simple inversion, or cove-shaped inversion. The electrocardiogram approached a normal form if the rheumatic infection cleared up, but in 1 case, even at the stage of complete recovery, there was persistence of isoelectricity of the T-waves. In none of the 3 cases was evidence of a pericardial effusion present, which fact is of interest in that some authors have held the belief that a complicating pericarditis might be responsible for the T-wave and R-T variations. These changes, though not pathognomonic for rheumatic fever, occur rather commonly, as shown in a review of the literature. Anatomical studies are cited which support the conception that the S-T (R-T) and T changes express an alteration of the musculature caused by the effects of the acute infection on the coronary circulation.

**HYPERTENSION.—ARTERIORLAR (ESSENTIAL) HYPERTENSION.—Incidence.**—To determine more clearly the presence of a familial or hereditary factor in arteriolar (essential) hypertension, D. Lyman (Arch Int Med 53:792 (May) 1934) made a direct study of the blood-pressure, height and weight of 1524 members of 277 families. In 780 members, aged from 14 to 39 years, of the second generation of the families, elevated systolic and diastolic blood-pressure readings (140 systolic and 80 diastolic, or higher) occurred in 148 subjects. These 148 subjects had the same average age and sex incidence as the entire group of 780 children, but they were 14.3 lbs. above the average weight compared to 4.5 lbs. above the average weight for the normal children. In the

families whose parents had absolutely normal blood-pressures, the incidence of elevated blood-pressures in the children was only 3.1 per cent, whereas in the families in which 1 parent had arteriolar hypertension, the incidence of elevated readings in the children rose to 28.3 per cent, and in the families in which both parents had arteriolar hypertension, the incidence of elevated readings in the children reached the striking level of 45.5 per cent. Of 70 brothers and sisters of parents with normal blood-pressures, 37.3 per cent. had elevated blood-pressure readings, whereas of 86 brothers and sisters of parents with arteriolar hypertension, 65.3 per cent had elevated blood-pressure readings. Study of 18 families in which parts of 3 generations were available presented results strikingly similar to those just mentioned. The results of this study point to the existence of a hereditary factor in arteriolar (essential) hypertension.

**Treatment.**—*X-ray Therapy of Pituitary and Adrenals.*—In view of the relief afforded by x-ray therapy in what may be termed Cushing's syndrome, *i. e.*, pituitary basophilism, in which severe hypertension is present with certain other signs and symptoms, P. C. Baird, J. R. Lingley, and R. S. Palmer (New England J Med 211 952 (Nov 22) 1934) conceived the idea that x-ray treatment might have some favorable effect in severe forms of essential hypertension though not conforming strictly to the characteristics of that syndrome. However, in a study of 8 patients with severe essential hypertension, in the late stages of the disease, treated by x-ray radiation over the pituitary or adrenals or both over a period of 2 years, no strikingly favorable results on blood-pressure or symptoms were found with the dosage used.

**THYROTOXIC HYPERTENSION.**—**Treatment.**—The common occurrence of thyrotoxicosis in patients having essential hypertension has been investigated by J. Parkinson and C. Hoyle (Lancet 2·909 (Oct. 27) 1934). Two-thirds of these patients have had a chronic goiter for many years, and at least one-half of them have also manifested chronic thyrotoxicosis. The patients are usually women between the ages of 45 and 65 years, they are thin, excitable and easily tired. Enlargement of the thyroid gland may be minimal, even doubtful, occasionally it is substernal. The tachycardia is 90 to 110; the systolic blood-pressure is between 170 and 240, often with a low diastolic figure (high pulse pressure). Paroxysms of auricular fibrillation may be followed by permanent fibrillation. In any patient with hypertension showing tachycardia, and still more if there is auricular fibrillation with or without cardiac failure, the thyroid gland should be examined most critically and supporting evidence of hyperthyroidism should be sought. Thyroid hypertension calls for special consideration in treatment. Thyroid extract is contraindicated. If iodine or iodide is used for hypertension, its possible effect on an abnormal thyroid should be taken into account. Subtotal **thyroidectomy** will often relieve symptoms, and prevent or dispel auricular fibrillation which so often determines a premature heart failure in hypertension.

**NEUROCIRCULATORY ASTHENIA.**—Neurocirculatory asthenia is of great importance because of its frequency, because of the marked suffering and even invalidism that it may cause, and especially because of the need for its



proper recognition and early treatment. This syndrome must be distinguished from irritability of the heart alone shown by premature beats or paroxysmal tachycardia and also from psychoneurosis as such, in which anxiety, hypochondriasis or hysteria is predominant. In an effort to throw more light on certain aspects of neurocirculatory asthenia (in particular, its etiology and symptoms), H. R. Craig and P. D. White (Arch Int Med 53:633 (May) 1934) analyzed 100 cases, 50 without and 50 with organic heart disease. The females outnumbered the males 69 to 31. Ninety-eight of the patients were white and 2 were negroes. The ages ranged from 12 to 69 years, the average age being  $35\frac{3}{4}$  years ( $31\frac{1}{2}$  years for those with pure neurocirculatory asthenia and 40 years for those with complicating organic heart disease). The great majority of the patients were well developed and well nourished, or obese. Only 9 per cent were poorly developed or undernourished. Ninety-one per cent had sedentary occupations, while only 9 per cent performed laborious tasks.

**Etiology.**—The factors initiating symptoms or contributing to them are numerous. In the group presenting a definite neurogenic element are encountered many individuals in whom symptoms of neurocirculatory asthenia develop on slight provocation, while in others the symptoms develop only after many trying experiences. However, many of the persons of the neurocirculatory asthenic group are definitely neurotic or psychoneurotic, as noted by M. A. Rothschild (Bull New York Acad Med 6:223 (Apr) 1930) and others. Craig and White (*loc cit*) believe that definite neurogenic elements can be discovered in at least 75 or 80 per cent of these patients if sufficiently investigated. As stated by F. P. Boas (Am J M Sc 176:789 (Dec) 1928), "the anxiety neurosis, and the varied psychic disturbances that contribute so largely to the development of the picture of neurocirculatory asthenia may be regarded as producing excessive and exaggerated stimuli which reflexly affect the heart through the corticomedullary pathways, whose course is still unknown." Such a factor as anxiety over family, finances or disease is often contributory. Sexual irregularities, such as maladjustment, overindulgence or an unhappy marriage, may be an evidence of the neurogenic element. In several patients with changes due to pregnancy or the menopause, the physiologic processes were found to upset the delicate balance of persons previously considered normal and to initiate symptoms of neurocirculatory asthenia. Infectious diseases or operations are at times responsible for the onset of symptoms. Nearly one-half (44 per cent) of the patients suffered from some functional gastrointestinal complaint, varying from occasional nausea, vomiting, or heart-burn to frequent episodes of severe abdominal distress, which in no case proved after careful study to be of organic origin.

Coffee, tea, alcohol, and tobacco are not looked upon as causes of neurocirculatory asthenia, although they may be aggravating factors, and it was found that persons with, or subject to, neurocirculatory asthenia indulge in these things less than individuals without neurocirculatory asthenia.

Disease of the thyroid gland had occurred as a past event in 2 of the 100 patients—thyrotoxicosis in 1 in the group with pure neurocirculatory asthenia, and colloid adenoma in the other in the group complicating organic heart disease. In both cases, the neurocirculatory asthenia continued with little or no improve-



ment after the disease of the thyroid gland had been eradicated Effort syndrome simulating neurocirculatory asthenia is the rule when thyrotoxicosis is present.

Neurocirculatory asthenia may be classified *etiologically*, as follows:

"Type A:

1. That which follows severe infection, operation, or other illness
- 2 That following prolonged, fatiguing work or strain of some other sort without respite.

"Type B

- 1 That following a slight to moderate infection, operation or other illness
- 2 That following a moderate amount of fatiguing work or a strain of any sort.

"Type C

That occurring after little or no strain, but much aggravated by illness or fatigue.

A (1) and (2) may occur in people with normal constitutions, B (1) and (2) in the borderline group, and C in those who are definitely inferior constitutionally There may be combinations of A (1) and (2), A (1) and B (2), B (1) and (2), or B (1) and A (2).

According to this classification, 9 per cent of our patients belonged to group A (1) and 10 per cent to A (2), while 61 per cent. belonged to group B and 20 per cent to group C "

**Symptoms and Signs.**—Palpitation, respiratory discomfort, precordial pains or aches, and exhaustion are the 4 cardinal symptoms of neurocirculatory asthenia They occurred with almost the same frequency in the order named in 73 to 78 per cent of the 100 patients Other symptoms, often or sometimes present, are faintness, syncope, insomnia, headache, dizziness, increased perspiration, difficulty in swallowing, tremor, flushing and pallor *Palpitation* usually consisted of the subjective sensation of pounding or of forceful beating of the heart at either a normal or a rapid rate Occasionally a patient with pure neurocirculatory asthenia complained of irregular palpitation, but, for the most part, it was described as fast and regular Premature beats were infrequent in the cases of pure neurocirculatory asthenia (once in 50 cases), but they may occur with regularity, even producing a bigeminal rhythm of the pulse *Respiratory discomfort* or even actual dyspnea was the second most common symptom (77 per cent ), and, like palpitation, it was more often subjective than objective, being an unpleasant consciousness of the ordinary respiratory act without much evident labor, distress or rapidity of respiration The dyspnea may occur during rest, but more often it comes on after excitement or from slight to moderate exertion If the dyspnea occurs at rest, the patient usually states that he feels as though not enough air were getting into the lungs and that, therefore, it is necessary to take a long breath, which is often evidenced by a deep, sighing inspiration This is a useful sign in confirming the diagnosis of neurocirculatory asthenia *Sighing* was present in 35 per cent of the cases of the present series, and it was noted in 80 per cent of 100 other cases studied by R D White and R G Hahn (Am J M Sc 177-179 (Feb ) 1929) During rest the respiratory rate is usually normal or only slightly increased in rate, while after exercise it is often increased out of proportion to the amount of exertion, and may be much shallower than normal Often a patient will complain that he has had to give up some sport because of shortness of breath on exertion *Precordial pain or discomfort* occurred in 74 per cent of the patients, somewhat more commonly in those with organic heart disease (84 per cent. in contrast to the 64 per cent of the patients without organic

heart disease). It varied from an occasional "heartache," usually a constant dull aching or burning sensation, to the sharp, needle-like pain which lasts a few seconds, but which may recur over periods of minutes to hours. The location, character, and duration of the pain or discomfort clearly distinguish it from angina pectoris. Radiation of the precordial discomfort to the left arm, axilla, shoulder, scapula, or even to the right arm, may occur (as in 33 of 74 patients of this series). The more severe the discomfort, the more likely the radiation. *Exhaustion or easy fatigability* may be constant or intermittent, occurring only at the time of, or sometimes apparently initiating, an episode of neurocirculatory asthenia. Exertion or emotional strain seems to increase the ease of fatigability.

According to T. Lewis ("The Soldier's Heart and the Effort Syndrome," Paul B. Hoeber, Inc., New York, 1919), *syncope* occurs not infrequently with "the effort syndrome" (neurocirculatory asthenia), while others believe that it occurs only rarely. It was noted in 19 per cent of the patients in this series, but in them not often, as a rule, in a few cases it happened frequently, even up to several times a week. *Faintness* is a much more frequent symptom than syncope, having been found in 38 per cent of the two groups. It may occur after emotional strain or may be present only when the patient experiences some of the cardinal symptoms of neurocirculatory asthenia. It is also accompanied by dizziness, and it may or may not precede syncope. The symptom of *increased perspiration* occurred in 18 per cent of the cases, *tremor* in 13 per cent, *flushing* in 10 per cent, and *pallor* in 8 per cent; these may be considered as confirmatory symptoms of neurocirculatory asthenia, but when existing alone, they certainly are not diagnostic of it. *Insomnia* occurred in 30 per cent of the cases. Eleven patients complained of symptoms suggestive of *globus hystericus*, varying from a choking sensation when tired to a full-sized globus.

*Cardiac enlargement* was not present in any member of the group with pure neurocirculatory asthenia. However, 50 per cent of this group had "functional" systolic murmurs, for the most part apical, but often pulmonary, which were described as soft or faint. The murmurs were not increased after exercise and were usually lessened by deep inspiration. In 4 of 49 patients of this group the systolic *blood-pressure* was above 150 mm. of mercury on the first examination, while subsequent readings for the same patient showed the pressure to be much lower. The same variation was found to be true for the diastolic pressures. The *average systolic pressure* for this group was 129 mm. of mercury and the average diastolic 78 mm. Fifteen of the patients with pure neurocirculatory asthenia had *sino-auricular tachycardia* ranging in rate from 110 to 160, while 1 had *premature auricular beats* producing a bigeminy which reverted to normal rhythm after exercise. Eight patients had *diphasic T-waves* in Lead II with inverted T-waves in Lead III. Six obese patients had slight *left axis deviation*, and 5 well-developed and well-nourished patients had a tendency to *right axis deviation*. Five gave histories of *paroxysmal tachycardia*.

**Prognosis.**—In uncomplicated neurocirculatory asthenia the prognosis is always good as far as length of life is concerned. There is, however, some degree of incapacity, the amount depending upon several factors: the severity of the symptoms, the constitutional make-up of the patient and the intensity or adequacy

of the treatment. It should be borne in mind that with a return of the causative factors there will probably be a return of the symptoms, especially in classes B and C. In group A, the symptoms often cease permanently after an adequate rest or convalescence.

In a group of 601 patients with effort syndrome, studied over a period of 5 years by R. T. Grant (Heart 12.121 (June) 1925), 15.3 per cent recovered entirely, 17.8 per cent improved, 56.2 per cent remained stationary, and only 2 per cent became worse. The incidence of serious disease in this group was 8.7 per cent; the most frequent infection was tuberculosis (2.7 per cent.). Definite heart disease developed in only 1 per cent. As noted by P. D. White ("Heart Disease," The Macmillan Company, New York, 1931), there is a distinct tendency for persons with neurocirculatory asthenia to live partially crippled lives.

It is important to realize that, although an individual may have definite organic heart disease, his symptoms may be, and often are, entirely on a functional basis not originating in the heart lesion.

**Treatment.**—The most essential point in treatment is to take the patient wholly into one's confidence, to explain carefully the nature of the condition, to dispel all fears of heart disease or, if any disease is present, to explain the degree of limitation of activity necessary in view of the organic disease and also to explain that the symptoms are dependent on the neurocirculatory asthenia and not on the heart disease.

The plan of life of the patients should be worked out with care and understanding. Each patient should realize that he or she must live within certain limitations in order to avoid things that produce symptoms. Usually normal but quiet work and play are advisable, with avoidance of late hours, coffee, tea, over-indulgence in alcohol and tobacco, strenuous vacations, excitement in general, too many hours at work and undertaking new and burdensome tasks or duties. Often after a few follow-up visits over a period of a few months, the patient adjusts himself to his surroundings and has no further symptoms. In the more severe cases of groups B and C, either with a marked psychoneurosis or a definite constitutional defect, it may be wise to seek a consultation with a psychiatrist with the hope of clearing up emotional conflicts present. After this has been done, it is wise to follow the patient from the cardiac point of view, giving helpful reassurance regarding the heart. psychoanalysis alone will not cure.

Numerous drugs have been tried in the treatment of neurocirculatory asthenia, but, for the most part, they have been found to be of little value, except in very *nervous patients*, for whom mild sedatives, such as **bromides** or the **phenobarbital** derivatives, are often helpful in the symptomatic treatment. Whether or not **suprarenal sympathectomy** may prove to be of value cannot as yet be stated. **Reéducation** and **reassurance** are the keynotes of treatment. However, for the more severe cases, saturation with rest at the beginning is often advisable, with the prescription of proper rations of rest thereafter. Suitable **rationing of rest** is to be recommended for all cases.

**PERIPHERAL VASCULAR SYSTEM. — CAPILLARY PRESSURE AND CAPILLARY PERMEABILITY.**—In a comprehensive review

of capillary function, E M Landis (Physiol Rev 14.404 (July) 1934) states that the movement of fluid through the capillary wall depends primarily upon the balance between capillary blood-pressure and the colloid osmotic pressure of the blood. The effectiveness of this balance is modified, however, by endothelial damage, by tissue pressure, by temperature, by the accumulation of metabolic products and by other independent factors. The *total capillary surface* of an average man is approximately 6300 square meters. The capillary wall has the physical characteristics of an inert (in the sense of nonsecreting) membrane permeable to water and crystalloids, but relatively impermeable to the plasma proteins. The peripheral fall in blood-pressure does not cease at the junction of the arterioles and capillaries, but continues through the capillary network. In man, the *arterial capillary pressure* amounts, on the average, to 45 cm of water, *venous capillary pressure* to about 22 cm of water. The *colloid osmotic pressure* of human blood amounts to about 36 cm of water. Owing to the *gradient* of capillary pressure, under average conditions filtration is favored in the arteriolar portion of the capillary network, while absorption is favored in the venous portion. The height of capillary pressure depends upon arterial tone, freedom of venous outflow, posture and temperature—to mention only those factors which have been studied in detail. Blood-pressure in an entire capillary, or even in a whole network, may be at one moment far above, at another far below, colloid osmotic pressure of the blood, favoring massive filtration or massive reabsorption, respectively, over large areas of endothelium. Usually, but not always, arterial pressure and active hyperemia increase the filtration of fluid. Elevating venous pressure is also associated with increased filtration, the rate of filtration being proportional, within certain limits, to the venous pressure.

Analyses of edema fluid, blood and lymph indicate that the capillary wall is usually relatively *impermeable to protein*. In many tissues the endothelium normally retains at least 95 per cent of the total plasma protein. Generalizations should not be made to apply to all capillaries, since regional differences in permeability exist. The *exchange of diffusible solutes*, to which the capillary wall is more or less permeable, need not follow the current of water during either filtration or absorption. When the electrolyte equilibrium is disturbed, fluid movement is modified temporarily until diffusion equalizes the concentration and the osmotic pressure of the electrolytes inside and outside the capillary. The rates at which certain poorly diffusible dyes pass through the various portions of the capillary network indicate that the capillary wall becomes increasingly permeable to dyes toward its venous extremity. The greater passage of dyes through venous capillaries is independent of capillary pressure and fluid movement, and is presumably due to poor diffusion. Yet, elevating capillary pressure increases the passage of dyes everywhere along the capillary so that under appropriate conditions the filtration of dye-stained fluid may be superimposed upon poor diffusion of dye, and may even obliterate all evidence of local differences in endothelial permeability. *Tissue pressure* modifies the movement of fluid through the capillary wall and normally prevents excessive filtration. The available evi-

dence indicates that swelling of the tissues accounts for relatively little retention of fluid. Bound water is not present in sufficient quantity to modify the balance between the capillary blood and the tissue fluid appreciably. Innervation, hormones and calcium affect the movement of fluid and dissolved substances through the capillary wall, but their action cannot be ascribed definitely to changes in capillary permeability, since the observations are complicated by possible modifications of blood flow and particularly of capillary blood-pressure.

The effects of *heat* on fluid movement through the capillary wall are explicable on the basis of (a) capillary dilatation, which increases the area available for fluid movement; (b) rise in capillary pressure, which favors filtration, and (c) injury, by which heat, like other noxæ, increases capillary permeability to colloids and consequently lowers the effective osmotic pressure of the plasma proteins. *Functional activity of the tissues* produces hyperemia and with it a rise in capillary blood-pressure. The increased flow of lymph which accompanies tissue activity is probably too great to be explained on the basis of a simple rise in capillary pressure; it is likely that osmotically active substances produced in the course of tissue metabolism are concerned. The accumulation of carbon dioxide and changes in hydrogen ion concentration within physiological limits have little, if any, influence on capillary permeability, certainly not enough to lower the effective colloid osmotic pressure of the plasma proteins to any measurable extent. Lack of oxygen, if extreme, can produce a temporary increase in permeability which is great enough to reduce the effective colloid osmotic pressure of the blood to half its normal value. Openings appearing temporarily in the capillary wall may explain certain anomalies of fluid movement observed during muscular activity. *Local injury* initiates a complex response, including vasodilatation, rise in capillary blood-pressure, first increased then decreased blood flow, increased endothelial permeability and finally stasis. All forms of local or general edema produced by injury are due fundamentally to increased capillary permeability with easy passage of proteins and water through the endothelium.

In conclusion, Landis states that many facts concerning fluid balance, particularly in the intact animal or in patients with clinical edema, cannot be explained in terms of the simple physical forces considered in this review. However, it seems probable that adequate control of these elementary forces will make the search for other factors both simpler and more productive, and the postulation of theories involving either active intervention of the endothelium or various modifications of its permeability under conditions inadequately controlled from the physical standpoint will not be necessary.

**BLOOD FLOW IN LUNG CAPILLARIES.**—In a study of the blood flow in the superficial pulmonary blood-vessels and air sacs in the unopened chest of the cat, microscopically, by transillumination,\* J. T. Wearn, A. C.

\* The lung was brought into view by dissecting away the muscle in the mid-axillary line between the eighth and ninth ribs until only the parietal pleura remained as a clear, transparent, intact membrane. Through a mid-line abdominal incision another window was made in the diaphragm, immediately opposite the one in the chest wall, by dissecting the muscle from the abdominal surface of the diaphragm until the pleura was exposed. A beam of light from an arc lamp was passed through a cooling temperature and a quartz rod, and thrown through the diaphragmatic window so as to transilluminate the tip of the lung and make possible observations of the pulmonary vessels with a Spencer binocular bi-objective microscope at the window in the chest wall.

Ernstene, A. W. Bromer, J. S. Barr, W. J. German and L. J. Zschiesche (Am. J. Physiol. 109. 236 (Aug.) 1934) observed intermittence of blood in the pulmonary arterioles, and the number of arterioles through which the blood circulated at a given time was found to be not constant. The rate and character of blood flow changed spontaneously or as the result of the injection of epinephrine and other substances. The number of capillaries through which blood flowed at a given time varied greatly. The velocity of blood flow and the cell content of the blood at times varied in capillaries arising from the same arteriole. Intermittence of blood flow, which was commonly observed in the capillaries, is believed to be the normal behavior of these vessels. Changes in the capillary flow are probably governed by changes in the arterioles from which they arise and by slight changes in the pressure in the pulmonary circuit. No proof of contraction of the capillary walls was obtained.

**PULSE OF FOOT.**—An erroneous diagnosis of peripheral vascular disease at times results from apparent but not actual absence of the pulses of the foot. R. S. Reich (Ann. Surg. 99. 613 (Apr.) 1934) studied the arterial pattern in 70 legs of 35 white cadavers. The following patterns of anomalous arterial circulation were found: (1) In 1 foot the anterior tibial artery subdivided into a larger tarsal artery and a smaller dorsalis pedis, and the arcuate artery was a branch of the lateral tarsal. In this case during life the dorsalis pedis pulse might easily have been overlooked because of the small caliber of the vessel, but pulse would have been palpable in the lateral tarsal artery over the lateral cuneiform bone. (2) In 2 specimens there was complete absence of the dorsalis pedis, the interosseous space being supplied in one of them by the dorsal arterial tree and in the other by the medial plantar artery. (3) In 2 feet the dorsalis pedis was not recognizable even as a loop, and the anterior tibial continued downward as a central channel greatly reduced in size. The dorsum of the foot was supplied by the plantar arteries and the pattern became quite complex, the channels being small and clinically nonpalpable. (4) In 6 specimens the anterior peroneal branch from the posterior tibial artery had an increasing participation in the supply of the dorsum of the foot. Reich concludes that the *dorsum of the foot* may derive its arterial supply (1) directly through the anterior tibial, (2) from the plantar vessels, or (3) indirectly from the posterior tibial artery through its anterior peroneal branch.

A study of the *posterior crural region* of the 70 legs revealed the following significant anomalies, each of which, however, occurred only once (1.5 per cent). In 1 specimen the popliteal artery bifurcated rather high into 2 branches, of which the peroneal artery was obviously the main branch, while the posterior tibial was considerably reduced in caliber and formed a long loop with the peroneal, which continued downward as a source of supply to the foot, taking the place of the posterior tibial branch. In another specimen the distribution was essentially the same, but the posterior tibial loop was much smaller and both channels were greatly reduced in size. Undoubtedly, this pattern would have caused difficulty in palpation during life. Another specimen showed complete attenuation of the posterior tibial loop except at the points where this loop joined the main arterial trunk formed by the posterior tibial, continuing as a very small

posterior tibial and still smaller peroneal branch. The author concludes that the vessels of the leg below the knee present a pattern of somewhat unstable character, altogether different from the constant and clear-cut picture presented in text-books.

Fifty-two (74 per cent.) of the limbs had prominent dorsalis pedis arteries; in 5 (7 per cent.), the lateral tarsal was the larger; in 10 (14 per cent.), the lateral tarsal was the main artery of the dorsum of the foot; in 7, the dorsalis pedis was very small, and in 3 it was entirely absent; in 5 (7 per cent.), the lateral tarsal artery was small, and in 3 (4.5 per cent.) entirely absent; and in 3 cases, both the dorsalis pedis and the lateral tarsal arteries were absent. In the 35 to 5 per cent of legs in which the posterior tibial artery is absent, there is no posterior pulse and in a further 3 per cent the pulse is very weak. Reich concludes that the dorsalis pedis artery can be palpated in from 75 to 80 per cent. of lower extremities, and the lateral tarsal in about 14 per cent. If the dorsalis pedis pulse is not found in its usual location, the examiner should feel for a pulse more laterally situated on the dorsum of the foot, approximately over the head of the third metatarsal bone.

Palpation of the pulses may be rendered difficult or impossible not only by arterial anomalies, but also by adiposity and edema. In addition, the ligamentum laciniatum, covering the posterior tibial artery as it proceeds downward around the malleolus, may conceal the pulse of this artery even if the vessel is normal. In discussing the application of his findings to the diagnosis of circulatory disease of the lower extremity below the knee, Reich says "The presence of pulses of the foot rules out circulatory disease; absence of the pulses of the foot is an important aid in diagnosis if supported by other more positive evidence, but in doubtful and borderline cases absence of the pulses of the foot must not be construed as a pathognomonic sign because of the relative frequency of obscured or irregularly placed foot pulses, a condition still more confusing by the presence of adiposity or edema."

**EFFECTS OF TOBACCO ON PERIPHERAL VASCULAR SYSTEM.**—The peripheral vascular reactions to the smoking of cigarettes, based on 90 experiments made at the New York Post-Graduate Hospital, have been reported by I S Wright and D Moffatt (*J A M A* 103 318 (Aug 4) 1934). The subjects were confirmed smokers in an average state of health, 4 groups of cigarettes were utilized; and for each test only 1 cigarette, or less, was used. In the great majority, the smoking of "standard cigarettes" was found to produce certain definite pharmacologic effects:

(A) A marked drop in surface temperature occurs at the tips of the fingers and toes, varying in different individuals with the same tobacco and in the same individual at different times. The average drop was  $5.3^{\circ}$  F.—the maximum  $15.5^{\circ}$  F. (Chart I). Surface temperature at the forehead and waist did not show a similar change.

(B) Slowing and stoppage of the blood flow in the capillaries of the nail fold were frequently observed.

The length of time an individual had been a smoker and the number of cigarettes habitually smoked daily had no determinable effect on the degree of

temperature drop. Some individuals showed marked toxic effects from smoking 1 cigarette under controlled conditions. In each instance, these were experienced smokers who ordinarily observe slight or no symptoms from smoking. Very slight, if any, difference could be noted between the effects of the standard, denicotinized and mentholated brands of cigarettes. No effects on the peripheral circulation were found following the smoking of "ashless filter paper cigarettes." No definite relationship between the degree of drop in peripheral surface temperature and the skin tests for tobacco and nicotine could be established. It is thought that the lack of symptoms noticed by experienced smokers, under usual conditions of smoking, is probably, at least in many instances, not due to the development of an immunity to the toxins of tobacco smoke, but rather to a conscious or sub-conscious control of the rate and depth of inhalation, which keeps the toxic

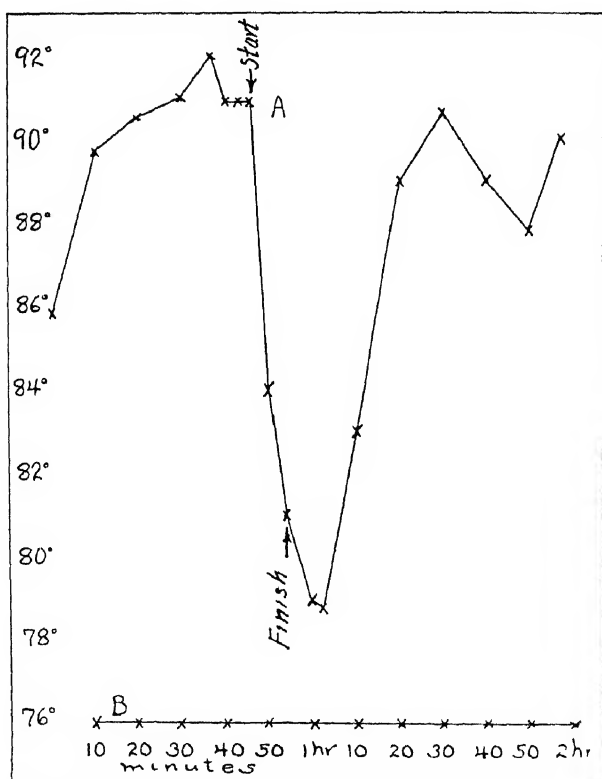


Chart I—Surface temperature curve at finger tips of a subject produced by smoking of a single "standard" cigarette (Cigarette III, patient G. W., Dec. 22, 1933); (A) fourth terminal phalanx, left hand, (B) 100m temperature (Wright and Mottatt) (J. A. M. A.)

effects at a submanifest level. Although not definitely proved the evidence seems to indicate that nicotine is at least one of the toxic factors and that carbon monoxide and the products of the cigarette papers may be eliminated as offending mediums. Tobacco itself varies widely in nicotine content; and the drier the tobacco, the greater the destruction of nicotine.

**PERIPHERAL CIRCULATION IN ACUTE LOBAR PNEUMONIA.**—After a study of the small vessels of the skin in 26 cases of lobar pneumonia, C. B. Perry (Quart. J. Med. 3: 273 (Apr.) 1934) concludes that an impairment in the efficiency of the contractibility of the capillaries occurs at the



height of the disease, and that circulatory failure is really a failure of the circulation at the periphery. Observations were made on skin color, blood-pressure, response of the skin vessels to histamine, to stroking and to adrenalin, and the back-pressure on the circulation required to obliterate the blanch produced by the latter. The blood-pressure is raised rather than lowered during the acute phase of the disease. In the majority of the nonfatal cases, the systolic pressure was higher before the crisis and fell immediately afterwards, the diastolic pressure was less affected by this change, so that the pulse pressure also fell after the crisis. Recovery of the capillaries is slow and not immediately affected by the crisis.

**PERIPHERAL VASCULAR DISEASE.—*Diagnosis and Treatment.***

—To determine the rigidity or flexibility of the vessels in patients with peripheral vascular disease, E. M. Landis (Ann. Int. Med. 8. 282 (Sept.) 1934) immerses the extremities in warm water. An elevation of skin temperature to  $31.5^{\circ}\text{C}$  ( $88.7^{\circ}\text{F}$ ) or more suggests that there is no significant arterial occlusion. When the maximum skin temperature, under the influence of the warm water, falls between  $26^{\circ}$  and  $31.5^{\circ}\text{C}$  ( $78.8^{\circ}$  and  $88.7^{\circ}\text{F}$ ), the patient has a moderate degree of organic occlusion. Patients in this class may be benefited by **physiotherapy**, **ganglionectomy**, and **vasodilating drugs**. When, in spite of the warm bath, the skin temperature fails to reach  $26^{\circ}\text{C}$  ( $78.8^{\circ}\text{F}$ ), the arteries are probably rigid or definitely occluded.

A method of treatment for patients with peripheral vascular disease is outlined. An aluminum box is provided fitting around the extremity, with air-tight cuffs at each end. By means of a mechanism of air-pumps, valves, and relays, with constant manometric control, the therapist produces alternations of pressure and suction. The extremity is exposed to a positive pressure of about 70 mm of mercury for 5 seconds, alternating with a negative pressure of about 100 mm of mercury for 25 seconds. This technic was employed on 16 patients with long-standing and advanced peripheral vascular disease. In 4 instances, the gangrene proceeded to the point of necessitating amputation. Best results were obtained in the patients who had indolent ulcers or large sloughs. These patients obtained striking relief from pain as a result of the **suction-pressure treatment**. Within a few days they were able to sleep without sedatives. Intermittent claudication was improved, but not markedly so. Even in cases of organic occlusion, the blood flow was increased during and for a short time after this treatment. Osteomyelitis is the principal contraindication.

**Local Treatment of Advanced Disease.**—In the local treatment of advanced peripheral vascular disease, I. Starr, Jr (Am. J. M. Sc. 187. 498 (Apr.) 1934) advocates the use of a **thermoregulated foot cradle**, since the optimum environmental temperature for relief of pain was found to be  $33$  to  $35^{\circ}\text{C}$  (approximately the same as that of the skin of the normal foot when the vessels are fully dilated). At higher temperatures the foot usually became bluer and pain, if present before, returned. "Baking" a foot with undiagnosed peripheral vascular disease may cause gangrene. **Oxygen** in concentrations above 80 per cent caused relief from pain and slowly developing change of color. Some cyanotic areas became bright arterial red, others showed less change and

in still others the cyanosis persisted. No change in skin temperature accompanied the changes in color, therefore, it is concluded that the effect must be due to penetration of oxygen into the blood and not to improved circulation. Judging by the relief of pain, it seems that lack of oxygen is one factor in the pain in gangrenous conditions. When oxygen was applied locally, it was found necessary to prevent the undue accumulation of moisture within the gas-tight cover. It soon appeared that this **desiccation** alone was of distinct advantage in preventing the development of wet gangrene, it may also convert a wet into a dry gangrene and so prevent infection of the necrotic area.

### **THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE).**

—**Etiology.**—As a result of biochemical and metabolic studies in a series of cases, H. J. Gray (Med. Bull. Veterans' Admin. 11: 16 (July) 1934) is inclined to believe that thromboangitis obliterans is due to intestinal putrefaction with a resultant toxemia. He suggests that the toxins in the blood stream have a selective affinity for the intima of blood-vessels. Tobacco may be a precipitating or aggravating factor, but is not a real etiologic agency.

**Diagnosis.**—The advent of thromboangitis obliterans is often suggested by certain prodromal signs, months and even years before the pain and claudication call attention to the disease. Among these early signs, Jean Marchak (Monde med. 44: 60 (Jan. 15) 1934) lists leukocytosis, diminution of sexual powers, weakness in the legs, brownish spots along the great veins of the lower extremities, tenderness in the course of the blood-vessels, increased blood cholesterol, and increased viscosity.

**Treatment.**—Marchak (*Ibid.*) is skeptical of the value of the usual forms of therapy, among those which afford only temporary relief, he lists **insulin**, **acetyl-choline hypertonic saline injections**, and **vasodilator drugs** by mouth. He warns that diathermy, and every other form of local heat treatment, are likely to aggravate the condition.

He believes that sufferers from this disease should not smoke, stating that no one of the patients in his series who insisted on continuing smoking ever improved. **Sodium nitrite** by injection is recommended, and its association with **ovarian extract** suggested. **Muscle tissue extracts** have given occasional favorable results and may be worth trying. **Ganglionectomy** is indicated in selected cases. Treatment of external iliac arteries with **phenol** may be used in conjunction with ganglionectomy.

Three or four types of treatment are available according to Gray (*loc. cit.*): (1) medical or drug treatment for mild and early cases, (2) **physiotherapy** for appropriate phases of all stages; (3) **sympathetic ganglionectomy** for cases of intermediate severity; (4) **vaccine treatment** for cases of intermediate severity—which the author prefers to ganglionectomy, and (5) **amputation** when gangrene becomes advanced or involvement extensive.

**Treatment of Gangrene.**—Three hundred cases of thromboangitis obliterans with only one amputation is the 8-year record of S. S. Samuels (J. A. M. A. 102: 436 (Feb. 10) 1934). On the basis of this record, the author insists that conservative treatment is an absolute duty, and that the mutilation of young men by ruthless amputation is a relic of medieval surgery. Ganglion-

ectomy has no place, and amputation very little place, in the modern treatment of Buerger's disease. Samuel's success in saving 299 out of 300 patients from amputation is ascribed to an adherence to the following therapeutic régime:

(1) **Rest in bed** is essential in order to put the limb in a horizontal position. If the patient, to relieve pain or for any other reason, is permitted to let the lower limb hang down, edema is quickly produced. Ambulatory treatment in a dispensary is likely to prove unsatisfactory because of the difficulty of maintaining a horizontal position in the legs of ambulatory patients. Through all phases of the ulceration and gangrene, this postural treatment is important.

(2) **Prohibition on smoking** must be enforced. Tobacco has a vasoconstrictor action, and smoking only aggravates the disease. A healthy granulating ulcer may change its appearance overnight if smoking is resumed. A demarcating area of gangrene may spread with florid rapidity with the resumption of smoking. With the cessation of smoking, there is usually a marked and spectacular decrease in the intensity of the pain.

(3) **Intravenous saline injections** should be started as soon as the diagnosis is made. The solution should be hypertonic, from 2 to 5 per cent; the dosage at each injection is 300 c c. An injection should be given every other day until healing of the ulcer or gangrenous area occurs.

(4) **Local treatment** of the gangrenous and ulcerative areas is required. **Foot-baths** of some mild antiseptic solution, lasting 10 minutes or more, followed by the application of an **anesthetic ointment** should be a daily routine. **Pain** should be treated with **milder sedatives**; opiates are rarely necessary, and when required **codeine** will usually be effective. Peripheral nerve section is contraindicated because of the danger of blunting the area to harmful stimuli.

A **sympathetic ganglionectomy** saved both upper extremities from amputation in a case observed by H. H. Stewart (Brit. M. J. 1 100 (Jan. 20) 1934). That gangrene would have probably set in was shown by the fact that the patient had lost both lower extremities because of an amputation necessitated by the extensive gangrene due to the thromboangitis. The inferior cervical and first thoracic ganglia were removed, the surgical approach being by way of the posterior route through the chest. No permanent ill-effects on the heart or on the cerebrospinal nervous system were noted.

**PULMONARY EMBOLUS.**—*Differential Diagnosis.*—*Acute Coronary Thrombosis*—Six cases, presumed to have had fatal attacks of coronary thrombosis, but in whom necropsy revealed that death had resulted from pulmonary embolization, are reported by S. H. Averbuck (Am. J. M. Sc. 187. 391 (Mar.) 1934). In 2 instances the diagnosis was extremely difficult in that coronary artery disease had previously been present. When the clinical picture suggesting coronary artery thrombosis occurs in a female patient who has neither arterial hypertension nor diabetes, a pulmonary embolus should be suspected. The high incidence of embolic phenomena in the female sex arising from **abnormal pelvic conditions** is an important factor in this connection. If the history suggests previous evidence of peripheral vascular involvement, *i. e.*, phlebitis, unilateral leg edema, pelvic disease, or lower extremity abnormalities, the likeli-

hood of the coronary syndrome being caused by an embolus to the lungs is strengthened. *Postoperatively*, the clinical picture of pulmonary embolus readily simulates coronary thrombosis; however, when it is recalled that pulmonary emboli are very frequent after operation and that coronary artery thrombosis is comparatively rare, because patients with coronary artery disease are spared any but emergency surgical procedures, such cases will be correctly analyzed. In a *hyposensitive* individual, when the diagnosis of coronary thrombosis is made in the absence of pain, and dyspnea is an outstanding sign, the possibility of a pulmonary embolus must be excluded. In pulmonary embolus the dyspnea is severe, taking the form of rapid stertorous breathing, signifying a genuine air hunger, and the cyanosis usually exceeds that of coronary artery thrombosis. X-ray films of the lungs always serve as an important means of determining the presence of pulmonary lesions, but, unfortunately, the gravity of the general condition of these patients usually contraindicates this procedure.

Pulmonary embolus usually induces a syndrome characterized by sudden painful oppression somewhere in the chest with *extreme cyanosis and dyspnea*. The pain has no typical radiation and often may be described as a strangling sensation, a sense of intrathoracic suffocation which provokes an *angor animi* as profound as that which occurs in angina pectoris or coronary thrombosis. In many cases shock accompanies the onset, and death occurs almost immediately. In those who survive the original shock, dyspnea, cyanosis, fever, and pulmonary râles with abnormal breathing constitute the clinical picture. In some cases the heart fails comparatively rapidly. Increasing cyanosis, hepatic congestion, and dilatation of the heart to the right signify right ventricular failure. Cough with sanguineous expectoration, pleural rubs and painful respiration depend upon the branch of the pulmonary artery and the area of lung involved. Recovery is not uncommon.

#### **RHEUMATIC HEART DISEASE.— INTRAUTERINE.**

Intra-uterine rheumatic fever is so rare that it is considered a historical curiosity. R. W. Kissane and R. A. Koons (Arch Int Med 52: 905 (Dec.) 1933) have reported the case of a child who was born with active rheumatic fever and a cardiac lesion. Throughout the entire pregnancy and at the time of delivery, the mother had active rheumatic fever with an elevated temperature and red, swollen, painful joints. During another pregnancy, 2 years later, she died, undelivered, of heart failure associated with an attack of rheumatic fever.

The child was born with red, painful, swollen joints, which caused him to cry out when gentle, passive motion was attempted. These facts were affirmed by the father and by the attending physician who also heard abnormal heart sounds and recognized the presence of a cardiac pathologic process on his first examination, 30 minutes after the infant's birth. At the age of 6 months the joint symptoms disappeared, and from that time there were no manifestations of active rheumatic fever. The child died at 9 years of age with the clinical diagnosis of rheumatic heart disease, cardiac hypertrophy and dilatation, myocardial insufficiency, panvalvulitis, mitral stenosis and insufficiency, tricuspid stenosis and heart failure.

At autopsy, there was marked edema of the entire body, ascites, pleural and pericardial effusion. The heart, when empty of blood, weighed 320 grams. Microscopic examination showed many Aschoff bodies scattered throughout the fairly well vascularized scar tissue which had produced tremendous thickening of the mitral valve leaflets. The aortic valve showed thickening, with a loose granular tissue covering its auricular surface. The leaflets of the tricuspid valve were compact, less vascular and thickened. The ventricles showed some increase in the intermuscular fibrous tissue, which was loose in character. The right auricle revealed an Aschoff body and considerable interfibrillar scar tissue.

**CORONARY ARTERIES IN.**—That coronary arteries are involved in rheumatic fever is an established fact, but the frequency of the lesions has been the subject of differences of opinion. Cardiac pain and discomfort are well-known symptoms in rheumatic fever, but proved coronary occlusion is a rare complication. With the thought that disease of the coronary twigs might be frequent and also that possibly adventitial and perivascular lesions might give rise to interference with the blood supply to the myocardium in rheumatic fever, H. T. Karsner and F. Bayless (*Am Heart J* 9: 557 (June) 1934) studied 56 hearts from recent autopsy material of Lakeside Hospital, Babies' and Children's Hospital and Cleveland City Hospital. Only hearts which showed Aschoff nodules or typical rheumatic inflammation were included. Of the 56 patients, 48 gave a history of rheumatic fever, except 1 who had chorea. Fifteen patients were in the first decade, 12 each in the second and third, 10 in the fourth and 7 in subsequent decades. There were 26 males and 30 females, 44 whites and 12 colored.

All cases showed *edema* of some part of the arterial tree. Chromotropic change was found to be about equally frequent in all decades except the second, in which one-third of the cases showed it as compared with about two-thirds in the other decades. Fibrinoid was found in all cases. *Necrosis* increased in frequency as age advanced, being observed in 40 per cent of the cases of the first decade, 50 per cent of the second, 75 per cent of the third, and 100 per cent subsequently. *Elastic alterations* were found in about 90 per cent of the cases in the first 2 decades and in all cases thereafter. *Aschoff nodules* in the adventitia were somewhat more frequent in the first 3 decades than in subsequent decades. Their invasion into the media was more frequent in the first 2 decades than later. *Infiltration of mononuclear cells* into the adventitia was observed in about two-thirds of the cases of the first 2 decades, about 90 per cent of those of the third and fourth decades, and in all the older cases. Infiltration into the media was present in 27 per cent of the cases of the first decade, 8 per cent of the second, 20 per cent of the fourth, and in none of the third, fifth and subsequent decades. *Thrombosis* was noted in the smaller arteries in 6 cases, in the capillaries in 1 case and in the veins in 14 cases, a total of 21 cases (37 per cent of the series). It was found in about one-half of the cases of the first 3 decades and in about 10 per cent of those of subsequent decades. *Fibrosis of the adventitia* was observed in 73 per cent of the cases of the first decade, 58 per cent of the second, 92 per cent of the third, and in all the cases in later periods. *Fibrosis of the media* was found in 26 per cent of the cases of the first decade, 17 per cent of the second decade, 33 per cent of the third, and 70 per



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## PLATE I

Fig 1—Edema of media, the so-called "*état reticulaire*," in a small epicardial coronary artery. Female, aged 2½ years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 150$ .

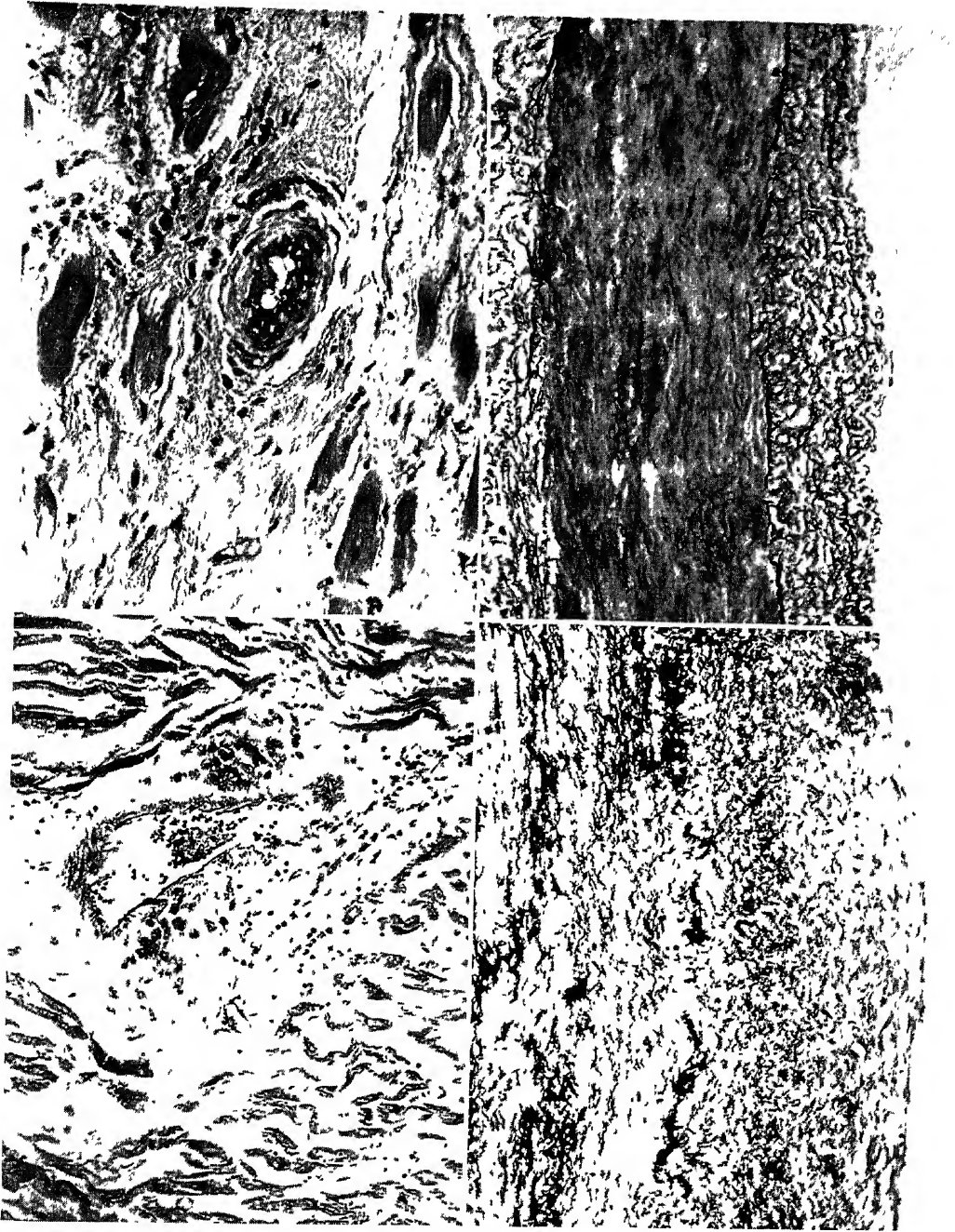
Fig 2—Edema of intima and media in large epicardial vein. Female, aged 20 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 215$ .

Fig 3—Necrosis in media of small intramural artery, with a small vacuolated area of edema. Male, aged 5 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 335$ .

Fig 4—Fibrinoid degeneration in upper media of large coronary artery, with many nodal points. Female, aged 35 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 230$ . (Karsner and Bayless. *Am Heart J*)

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## PLATE II

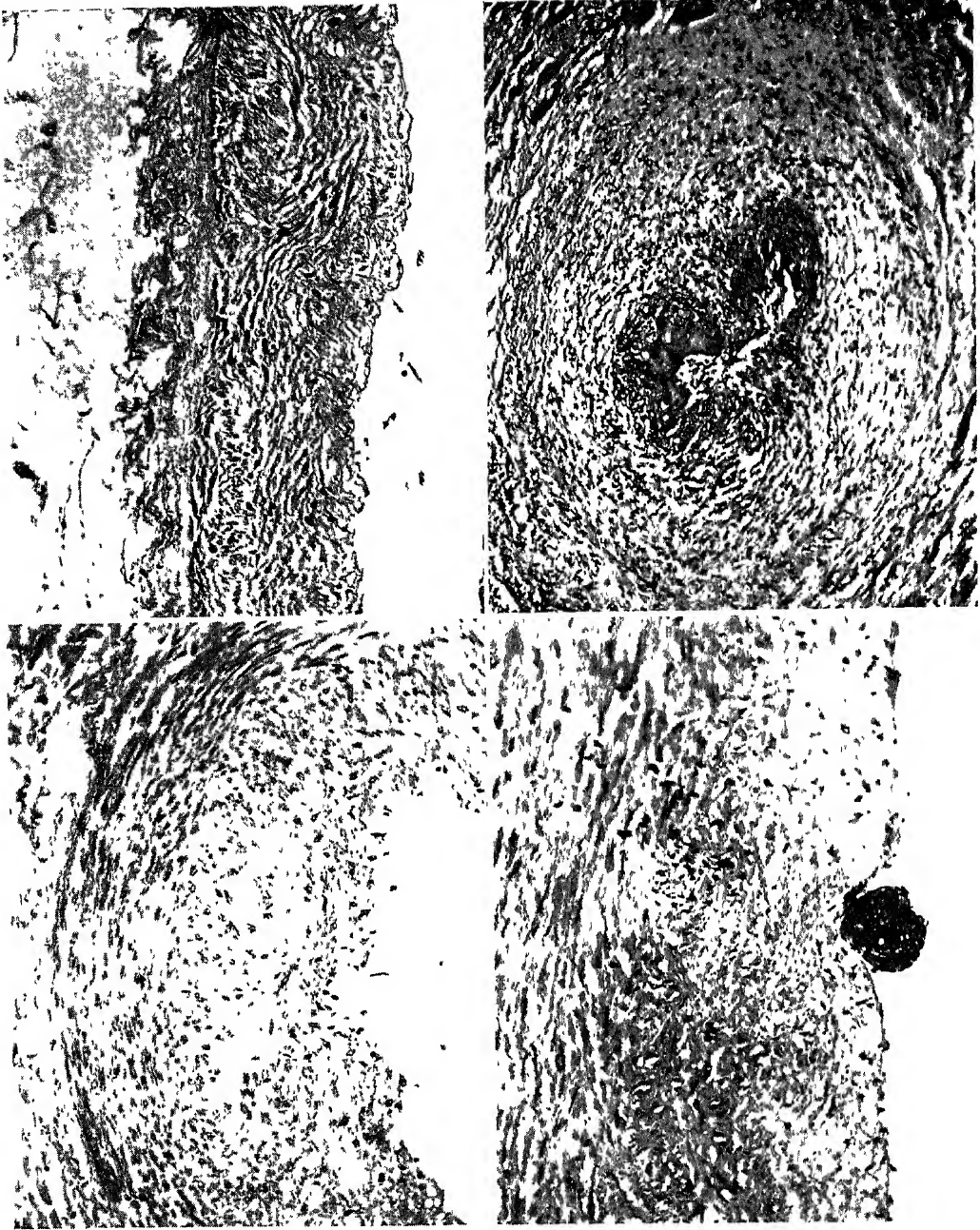
Fig 5—Swelling, fragmentation and fraying of elastica in large coronary artery. Female, aged 18 years. Voerhoff elastica. Wratten orange filter G-15.  $\times 165$

Fig 6—Marked swelling and fragmentation of elastica in large coronary artery. Female, aged 32 years. Voerhoff elastica. Wratten orange filter G-15.  $\times 165$

Fig 7—Marked swelling and wrinkling of elastica in small intramural coronary artery, with apparent reduction of lumen. Male, aged 29 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 230$

Fig 8—Aschoff nodules involving adventitia in a small intramural coronary artery. Male, aged 7 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 140$  (Karsner and Bayless. Am Heart J)





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PLATE III

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Fig. 9—Exudative inflammation of medium-sized intramural coronary artery. Female, aged 9 years. Adventitia shows fibrosis and polymorphonuclear leukocytes. Media shows fibrosis, edema, infiltration of polymorphonuclears and mononuclears. The intima is destroyed and shows cellular infiltration and marked fibrin formation. There is no organization of marginal fibrin and lumen contains erythrocytes. The process reduplicates the endocardial lesion of same heart. Clinically chorea. Hematoxylin and eosin. Wratten green filter B-58.  $\times 82$ .

Fig. 10—Mural fibrin thrombus attached to markedly thickened intima of large coronary artery. Male, aged 24 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 150$ .

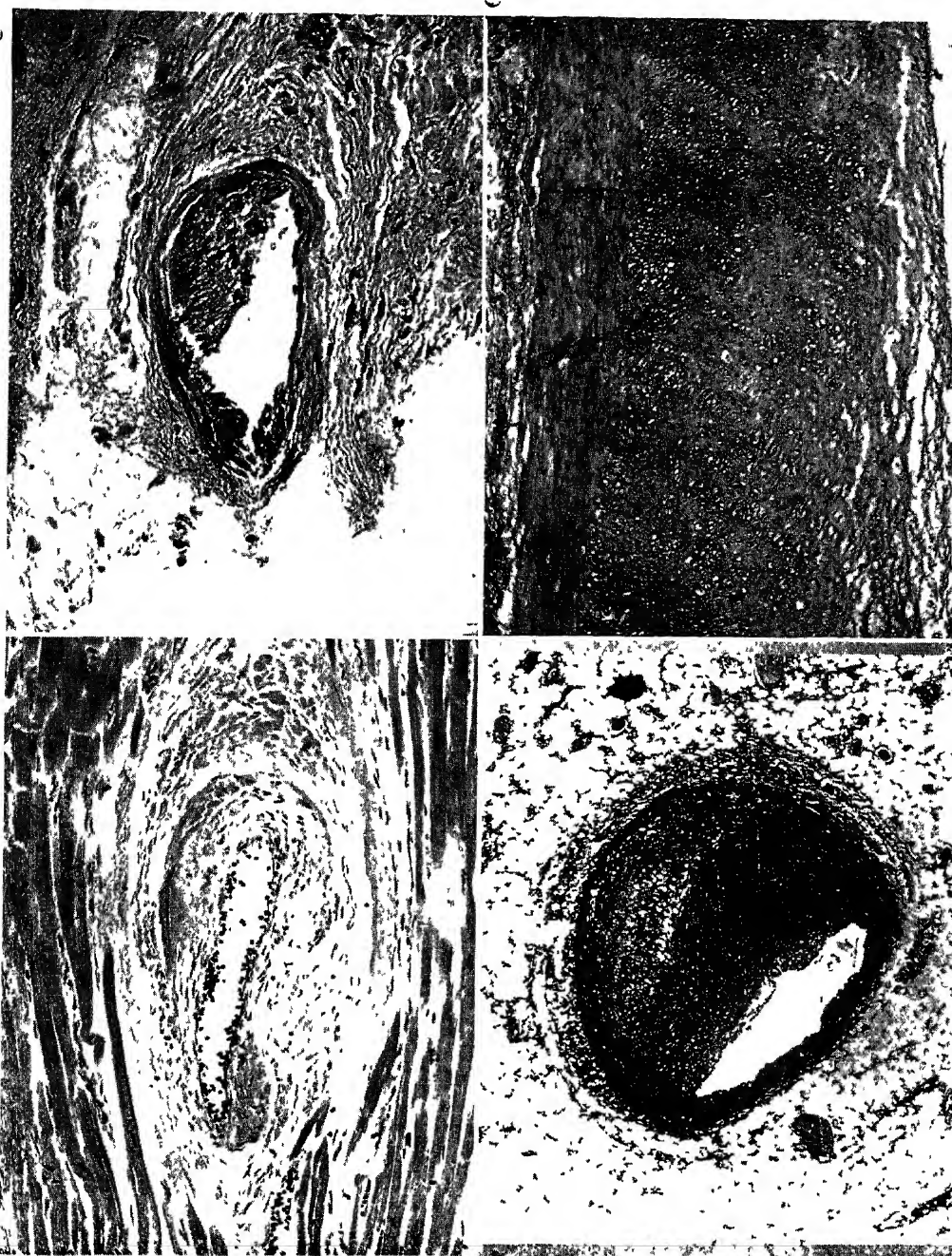
Fig. 11—Communicating fibrosis of intima and media with distortion of architecture (metallaxis) in large coronary. Female, aged 13 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 125$ .

Fig. 12—Marked fibrosis of intima with disorganization of media in large coronary. Female, aged 10 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 125$ . (Karsner and Bayless. *Am Heart J*.)



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## PLATE IV

Fig 13 —Marked fibrosis of intima of large coronary artery. Male, aged 24 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 65$

Fig 14 —Marked intimal sclerosis eccentrically situated in large coronary artery. Male, aged 19 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 17$

Fig 15 —Nodular intimal fibrosis, of a small intramural coronary artery. Female, aged 14 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 200$

Fig 16 —Irregular intimal and medial fibrosis with "hyaline scarring" of media in a medium-sized intramural coronary artery. Female, aged 43 years. Hematoxylin and eosin. Wratten green filter B-58.  $\times 120$  (Karsner and Bayless. Am Heart J)

cent of the fourth and subsequent decades. *Fibrosis of the intima* was noted in 73 per cent of the cases of the first decade, 92 per cent of the second, and all the cases of the third and subsequent decades. Of the cases in which notation was made, *grossly observable sclerosis of the coronaries* was found in 18 per cent of the first decade, 56 per cent in the second, 33 per cent. in the third, 66 per cent in the fourth, and all in the fifth and subsequent decades. Microscopically, severe *fibrosis of the intima of the large divisions of the coronaries* (when present in the sections) was observed in 38 per cent of the cases of the first decade, 50 per cent of the second, 70 per cent. of the fourth, and all the cases of the subsequent decades. Of 28 patients between the ages of 19 and 44 years inclusive, 5 showed sclerosis almost completely occlusive, all males, aged 19, 23, 29, 40 and 44 years, respectively.

Apparently, age has no influence upon edema, chromotropic change, fibrinoid or incidence of Aschoff nodules in the adventitia. With increase in age there was found an increased incidence of necrosis, elastica alterations, infiltration of mononuclear cells in adventitia, fibrosis of each coat of the arteries and grossly observable sclerosis. The incidence of thrombosis was markedly decreased after the third decade. Blood cultures showed no apparently significant relation between bacteremia and thrombosis. Of 10 cases from which streptococci were recovered, 5 showed thrombosis, and of 31 cases in which the blood culture showed no growth, 11 showed thrombosis. Of 12 cases from which organisms other than streptococci were isolated, none showed thrombosis.

In 40 *nonrheumatic hearts*, varying in age from 11 months to 58 years, examined as *controls*, *edema* and *necrosis* of some part of the coronary tree were observed in all cases. Chromotropic substance was not observed. Fibrinoid was found in 18 of the 40 specimens. In the first 2 decades, comprising 11 cases, *elastica change* was limited to slight swelling, and the youngest patient to show fragmentation or splitting was 24 years old. After that age, the more severe elastica lesions were found in 18 of 31 hearts. *Fibrosis of the intima* was found in only 1 of the 11 patients of the first 2 decades, in 2 of 10 patients of the third decade, in 6 of 10 of the fourth decade and in 7 of 9 in the fifth decade. *Fibrosis of the media* was found in 3 of 9 in the fifth decade. *Infiltration of mononuclear cells* was found in 1 case in the fourth decade. Gross sclerosis of the coronaries was found in 1 of the 5 cases of the first 2 decades where notation was made, in 2 of 5 of the third decade, in 2 of 5 of the fourth decade, in 4 of 5 of the fifth and sixth decades.

Karsner and Bayless believe that the edema which was constant in the rheumatic coronaries and in the controls, is probably due to the presence of infectious disease, circulatory disturbance or both. It was obviously more common in the media than elsewhere. It is not believed to be a postmortem artefact, but is probably in some way related to chromotropic substance. In the control cases, chromotropic change was not found in the coronary arteries, but it was observed in more than half of the rheumatic cases, in which it was almost equally common at all ages. Therefore, it was regarded as definitely pathological and not an age process alone. In this study, fibrinoid was considered to be an intensely acidophilic substance, arranged in fibrillar fashion, sometimes with beading at

intersections. It was observed in many of the controls, but was found in all the rheumatic cases. It was seen most frequently in the media, but was common in the intima and was found also in the adventitia. It is most frequent in arteries the seat of the supposedly allergic disturbances, but it may be found in other conditions. *Necrosis* was constant in the controls and appeared to be more frequent in the rheumatic series as age increased. Severe *elastica alterations* occurred earlier in the rheumatic group than in the controls. The infiltration into the adventitia of *large mononuclear cells*, evidently histiocytic in general character, and of those with the morphology of small lymphocytes and plasma cells, was frequent and practically constant after the third decade in the rheumatic cases, but was found in only one of the controls. Ante-mortem blood clots were looked upon as *thrombosis*, and were interpreted as being part of the vascular lesion rather than as emboli. In the smaller vessels this lesion was often occlusive, but in several larger vessels it occurred as a mural condition. In only one of the control cases was thrombosis present. However, it is not established that thrombosis is more frequent in rheumatic coronaries than in those of other severe infections. Microscopically, *fibrosis* was observed more often in the smaller arteries than in the main stems, which fact corresponds to the infrequency of gross sclerosis of the large arteries in the literature. By the end of the first decade more than two-thirds of the cases showed under the microscope intimal fibrosis of the smaller vessels, in the second decade, 92 per cent. exhibited it, and in the third and subsequent decades, it was present in all cases. Medial and adventitial fibrosis are more difficult to detect and occur less frequently. The controls showed intimal fibrosis in 1 of 9 cases of the first decade, none in the second, 2 of 10 in the third, 6 of 10 in the fourth, and all those of the subsequent decades. Medial and adventitial fibrosis were not found in the controls before the fifth decade. Thus, it is apparent that permanent disease appears in the coronary arteries early in the course of rheumatic fever.

The authors conclude that rheumatic fever regularly produces disease of the coronary arteries. Either inflammatory or fibrotic lesions, or both, are practically constant, but, with the exception of Aschoff nodules, the lesions are not specific for rheumatic fever. The disease predisposes to fibrosis of the coronary artery tree in early life and to what appears to be precocious coronary sclerosis. The coronary arteries undergo a progressive sequence of inflammatory lesions which closely resemble those of the endocardium and pericardium. It is practically certain that severe myocardial damage is associated with the arterial disease.

**TUBERCULOSIS, PULMONARY.**—*Axis Shift of Heart in Artificial Pneumothorax.*—In a study of 31 cases of pulmonary tuberculosis treated with artificial pneumothorax, 17 on the left and 14 on the right side, I. Treiger and C. J. Lundy (Am Rev Tuberculosis 29: 546 (May) 1934) found that in *uncomplicated* cases (without adhesions or fluid), a shift of the electrical axis to the *right* followed the operation. The degree of shifting was in direct proportion to the quality of the pneumothorax. The average shifting of the axis was greater in left than in right pneumothorax. In cases *complicated* by

adhesions or fluid, the electrical axis may be shifted to the *left*. The degree of shifting depends upon the location, quantity, and quality of the adhesions, and upon the quantity of fluid. Adhesions near the apex of heart (base of left lung) in left-pneumothorax cases were associated with both a shifting of the electrical axis and displacement of the heart to the left, which was in contradistinction to left pneumothorax before adhesions developed, which shifted the electrical axis and displaced the heart to the right. The shifting to the left is greater when the adhesions are numerous, strong and cord-like, and when pneumothorax is partial and of poor quality. The degree of shifting to the left is less when adhesions are few and weak and when pneumothorax is excellent and more complete. The adhesions interfere with the quality of pneumothorax and change it from complete and excellent into partial and of low grade. The location of the adhesions is important since adhesions in the base of the lung have their main influence on the cardiac apex. Only 1 case of right pneumothorax with adhesions was observed, this showed shifting of the electrical axis to the right with no gross change in the heart position after pneumothorax, but before adhesions developed, and after adhesions appeared, the electrical axis shifted slightly to the left and the heart position still remained unchanged.

Low voltage, less than 0.5 mv., in Lead I was observed in 13 of the 17 left-pneumothorax cases. Four of these were of low voltage before and remained so during pneumothorax, and 9 were normal before and of low voltage during pneumothorax. Low voltage of Q-R-S in Lead I was not observed in any right-pneumothorax cases. Low voltage of Q-R-S in Lead III was present before treatment in 3 left and 3 right pneumothoraces, all of whom developed normal voltage during pneumothorax. In both instances, when low voltage of Q-R-S appeared in Lead I and when low voltage of Q-R-S in Lead III returned to normal voltage, these changes accompanied shifting of the electrical axis to the right when determined by computation.

**Heart After Phrenic-Nerve Interruption** - In a study of 100 cases of pulmonary tuberculosis by O. S. Hansen and H. W. Maly (*Ibid.* 30: 527 (Nov.) 1934) before and after unilateral diaphragmatic paralysis by phrenic-nerve interruption for the production of pulmonary collapse, 52 operations were performed on the left side and 48 on the right. Electrocardiograms showed a change in the direction and amplitude of the Q-R-S waves in 65, slight in degree in all but 10, but enough to indicate a shift of the electrical axis toward the left in 25 (all but one after a left-sided operation), and toward the right in 10 (all but one after a right-sided operation). Only 6 cases showed any changes in the P-wave after operation, 3 an increase, and 3 a decrease in amplitude. No evidence of auriculoventricular conduction delay appeared. T-wave changes appeared in 23 cases, 10 showing an increased negativity in the significant leads and 13 an increase of size or a decrease of negativity. No clinical or x-ray evidence of myocardial change appeared, or of defective conduction through the ventricles. In 69 cases the heart was displaced from its preoperative position. After right-sided operations there was a preponderance of shifting toward the left or healthy side (29 of 30 cases). After left-sided operations the heart might be displaced to either side (15 toward the left and 17 toward the right).

# Endocrinology

*by*

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**ADDISON'S DISEASE.**—The diagnosis and treatment of Addison's disease with reference to a series of 46 patients treated with the **suprarenal cortical hormone** are discussed at length by A. M. Snell (Internat. Clin. 3:46 (Sept.) 1934). The first 20 cases of this series have been reported in detail by Rowntree, Greene, Ball, Swingle and Pfiffner. Thirty of these patients have died; 2 were admitted *in extremis* and no treatment could have been of avail; 4 deaths were clearly due to the patients' discontinuance of treatment at home, either because of neglect or because the hormone was not available. Twelve of the remaining 24 cases were earlier in the series and received various amounts of hormone only intermittently, and did not have the advantage of continuous treatment with extracts of known potency. In the other 12 cases, chiefly patients who had been under care at the clinic in 1932, treatment was presumably adequate, liberal amounts of an active hormone having been used more or less continuously. These last 12 cases are the most disappointing of the series, since results were unsuccessful in spite of the best available treatment. In 4 of these cases autopsy was performed and in each case an advanced degree of atrophy of the suprarenal glands was noted.

Atrophy has been noted much more frequently at necropsy since treatment with the cortical hormone has become an established practice. In 30 recent post-mortem examinations (22 reviewed from recent literature and 8 of this series), in 17 cases atrophy of the suprarenal gland was present and in only 13 was tuberculosis found. This is, of course, a considerable variation from the usual figures, which indicate that in about 80 per cent of cases the suprarenal lesion is tuberculous. There is no reason to believe that the use of the hormone induces atrophy of the gland. It seems more likely that among many patients with tuberculous suprarenal glands, there are small fragments of cortical tissue which may sustain life with the assistance of moderate amounts of cortical hormone, whereas in advanced states of atrophy a more complete degree of suprarenal insufficiency is present, and the patient must depend almost entirely on administration of cortical hormone to maintain life.

Sixteen patients of this series of 46 cases are alive, 7 of whom are in reasonably good condition 1 year or more after treatment with the cortical hormone was begun. Three patients are in failing health, and at least 2 of them feel that their present poor condition is due to their inability to supply themselves with an adequate amount of the hormone. Four patients have been under treatment for less than 6 months and are in good condition. Two patients have temporarily discontinued treatment; they are known to be living, but recent reports on their condition are not available.

Four strikingly successful cases in this group deserve especial comment. One patient, a youth aged 18 years, who has been under treatment for 2 years, is in excellent condition and is able to do light work. The second patient, a man aged 43 years, has passed through 2 periods of crisis and is still carrying on with his work as an engineer. The third patient, who was carried through an extremely severe crisis more than a year ago, has since been in a reasonably good state of

health The fourth patient, a man in the sixth decade of life, has been tided through a severe streptococcic infection by the use of the hormone and is at present working as a jailer. In a recent report he stated that he was able to engage in physical combat with some of his charges without harmful effect Three of these patients require small, frequent doses of the cortical hormone (approximately 2 c c —  $\frac{1}{2}$  dram—daily); the fourth patient is using considerably larger amounts; all are in the habit of increasing the dosage if respiratory infections, fatigue, and other emergencies develop

It is interesting to compare the periods of survival in a series of patients treated with the cortical hormone with those of a group treated prior to isolation and use of the hormone In a group of proved cases reported by Rowntree and Snell, in which the hormone was not used, the average duration of life of 26 patients with tuberculosis of the suprarenal glands was slightly less than 1 year after symptoms had first been noted; in a group of 6 cases with atrophy of the suprarenal glands, time of survival after symptoms had first been noted was 26 months Guttman, using statistical methods in a larger series, gave the average duration of life in cases of tuberculosis of the suprarenal glands as 13.3 plus or minus 2.55 months after appearance of symptoms and for atrophy 3.4 plus or minus 4.4 months In a group of 24 fatal cases which had been treated by means of the cortical hormone, the average duration of life after development of symptoms was 19 months, if 2 patients with histologically verified suprarenal atrophy who lived considerably longer than others in the group are excluded, this figure falls to 16 months On the basis of these data, it is apparent that the use of the hormone has not as yet greatly prolonged life on the average It must be said, however, that many of these patients had only insufficient supplies of the hormone and that many times the potency of the preparation was low A more hopeful aspect of the matter is that a group of 16 patients lived for more than 1 year after treatment with the hormone was first instituted, 8 of these died after 1 year or more of treatment and are included in the previously mentioned group, 8 are still living, and the 4 patients referred to in the foregoing paragraph are in very satisfactory condition

These results are, of course, less favorable than the theoretic expectation and yet they mark a distinct advance Even if the hormone has not so far greatly prolonged the average expectancy of life in cases of Addison's disease, it has greatly reduced the misery of the patients, and has brought a substantial number of them from a state of chronic invalidism to a reasonable degree of health This reduction in morbidity alone makes treatment decidedly worth while It is also reasonably certain that treatment with the hormone will greatly reduce the number of deaths from complicating diseases, especially those of an infectious nature, and will permit necessary surgical procedures in cases of Addison's disease To what extent the ultimate fatal prognosis will be altered is as yet uncertain Whether failures in treatment are due to inadequacy in the amount and potency of hormone administered, to lack of other essential substances, or to changes produced in other organs by long-continued partial insufficiency in the supply of the hormone, at present can only be surmised Many investigators are inclined to the belief that the first-mentioned supposition is correct The rate



and manner of the destruction of the hormone in the body may be the deciding factor.

The question may be raised as to the possibility of indefinite survival in cases of Addison's disease if the patients are given an unlimited supply of cortical hormone and are free from complicating disease. With experimental animals which have been subjected to bilateral suprarenalectomy, indefinite survival is being accomplished. The patient with Addison's disease is not strictly comparable to such animals, however. In the animals, the condition is an acute, absolute suprarenal insufficiency in an otherwise intact organism: in Addison's disease, the condition is a slowly progressive and partial insufficiency, which, in the process of development, may be associated with irreversible changes in other essential organs. Laboratory animals exist in a selected and controlled environment where requirements for additional hormone may be anticipated and met, this is not always possible for human beings. The probability is that eventually patients with uncomplicated Addison's disease will be able to live for long periods on substitution therapy, always subject to danger from trauma, infection, and other strains and stresses to which the human organism is constantly exposed, and which the person affected will be poorly equipped to combat because of the nature of his disease. The physician entrusted with the care of patients with Addison's disease should, Snell believes, regard the problem in an optimistic light, and consider indefinite survival as a possibility which is not completely beyond attainment. The methods of treatment now available, while admittedly imperfect, are capable of producing better results. The principal stumbling blocks are, of course, a lack of any measure of suprarenal function, and also the lack of any criterion by which the physiologic effects of the cortical hormone may be accurately determined. The rapid advances in the past 3 years seem to indicate that these obstacles may finally be overcome, and that the patient with diseased suprarenal bodies may have as effective a remedy by means of the cortical hormone as the diabetic patient has by means of insulin.

#### **ADRENALS. — CHRONIC SUPRARENAL INSUFFICIENCY. —**

In 1933, Maurice Packard and H. F. Wechsler (*Am. J. M. Sc.* 186: 66 (July) 1933) reported a case of malnutritional edema which exhibited a unique clinical syndrome and a degenerative lesion of the suprarenal glands at autopsy. The outstanding features of the syndrome were extreme emaciation, with complete loss of body fat, asthenia, anorexia, polyneuritis, trophic ulcers, a high level of nonprotein nitrogen in the blood, absence of pigmentation and hypotension. It was suggested that the syndrome was that of chronic suprarenal insufficiency, analogous to the similar state in animals produced by bilateral suprarenalectomy.

That chronic suprarenal insufficiency is not a rare condition is shown by the fact that these authors are now able to report 3 additional cases, 2 of which have come to autopsy (*Arch. Int. Med.* 54: 18 (July) 1934). Three of the patients were men and 1 a woman. The respective ages were 50, 53, 68, and 39 years. Malnutrition was the apparent etiologic factor in 3 cases. In 1 patient the suprarenal glands were involved by a metastatic carcinoma. Addison recog-

nized 3 causes of the disease which bears his name, *viz*, tuberculosis, atrophy and carcinoma

There were 2 significant findings at autopsy: an extreme to complete loss of body fat, accompanied by atrophy of the internal organs and a suprarenal lesion. The loss of fat was striking, involving not only the panniculus adiposus but also the internal fat depots. In the cases associated with malnutrition, the suprarenal lesion was one of hypertrophy and degeneration. The latter change was evidenced by vacuolar degeneration of the cortical cells, with areas of necrosis and regeneration and hyperemia, edema, hemorrhages, and capillary and venous thromboses of the interstitial tissue. What may have served as a contributory factor in 1 of the cases was the practically complete destruction of the right suprarenal capsule by idiopathic suprarenal atrophy.

The early *symptoms* of the disease are profound anorexia, marked weakness, apathy and progressive loss in weight. There is no pigmentation of the skin or visible mucous membranes. The wasting is extreme, and may continue until there is a complete loss of the body fat, the skin, however, retains its elasticity. The aversion to food is continuous and is not limited to any particular type, it is not accompanied by nausea, retching, or vomiting. The disposition alters completely, the patient becoming increasingly morose, lethargic and desirous of death. Pains, paresthesias and weakness in the extremities develop, and the signs of polyneuritis, such as tenderness of the nerve trunks, diminution or absence of reflexes, areas of anesthesia and paresis of the limbs, become manifest. Trophic ulcers also make their appearance in spite of every precaution. The patient becomes delirious, and tremulous and athetoid movements are noted. Death is due to bronchopneumonia. The course is afebrile, except for the onset of the terminal illness, and the final temperature is usually subnormal.

The disease must be differentiated from Addison's disease and pituitary cachexia. The absence of many of the cardinal features, especially pigmentation and hypotension, plus the appearance of additional factors, such as the practically complete loss of body fat, polyneuritis and trophic ulcers, sufficiently differentiate Addison's disease and chronic adrenal insufficiency.

Pituitary cachexia offers little difficulty in the *differential diagnosis*, as the disease runs an exquisitely chronic course, and the emaciation is accompanied by wrinkling of the skin, falling out of the hair and teeth, and atrophy of the genitalia. In multiple sclerosis of the endocrine glands, symptoms of both myxedema and suprarenal insufficiency are added to those of pituitary cachexia.

**Therapy.**—In only 1 case has specific therapy been attempted. With the use of a proprietary preparation of the **cortical hormone** and a diet high in **vitamin B**, encouraging results are being obtained.

**TUMOR OF ADRENAL CORTEX, FUNCTIONAL.**—**Diagnosis.**—**Test**—A typical case, diagnosed as "basophilic adenoma" was under the observation of R. T. Frank (Proc. Soc. Exper. Biol. and Med. 31: 1204 (June) 1934) for 1½ years during which time thorough hormonal studies were performed with extremely striking findings. This patient died suddenly in consequence of an erysipelas secondary to an acute middle ear infection (unoperated),

permitting a full autopsy. At autopsy, the pituitary was found normal, the basophilic elements proved to be diminished in number. A large carcinoma of the adrenal cortex was found.

Hormonal examination, extending over a period of 4 weeks, showed negative pregnancy tests, no increase in the prepituitary and female sex hormones circulating in the blood. On the other hand, the excretion of female sex hormone in the urine was at times tremendously increased, to a degree seen normally only in pregnancy (13,000 mouse units per liter). During what corresponded to 1 cycle, this patient excreted more than 57,000 mouse units of female sex hormone (estrin). It was repeatedly possible to obtain a mouse reaction with as little as a total of 0.075 c.c. of undiluted urine 48 hours after injection into the castrated mouse.

In another case studied, in which the patient presented the cardinal symptoms of "basophilic adenoma," the undiluted urine likewise gave a strong female sex hormone reaction in quantities of 0.2 c.c. (5000 mouse units per liter). At autopsy, no basophilic adenoma of the hypophysis was found, but a large carcinoma of the adrenal cortex with metastases in the liver was encountered. Extracts made from the primary and secondary tumor in the liver showed twice as much female sex hormone in the extracts, as in control tissues, such as the spleen.

Frank has had occasion further to test a number of other patients who have shown at least some of the symptoms ascribed to basophil adenoma of the pituitary without encountering the same high urinary findings of female sex hormone as in the 2 cases of undoubted cortical tumor. As these patients have not been operated upon and are still alive, they do not enable him to draw further conclusions.

Because of the rarity of the "basophilic pituitary adenoma" the author feels justified in drawing the attention of the profession to the hormonal findings obtained in these 2 clearcut cases, with the hope that this test (high female sex hormone excretion in the absence of positive pregnancy reaction) may serve as a means of recognizing adrenal cortical tumors at an early and operable stage. Perhaps this test will also serve in differentiating them from the "basophilic pituitary adenomas" if further observations prove that their presence does not produce the same overexcretion.

**AMENORRHEA.—Treatment.**—In the past year several reports have appeared in which the authors have succeeded in bringing about menstrual hemorrhage in castrated women by the administration of huge amounts of ovarian hormones. A. Loeser (J. Obst. and Gynaec. Brit. Emp. 41: 86 (Feb.) 1934) has treated 5 cases of primary amenorrhea with enormous doses of follicular hormone and succeeded in producing normal menstruation with doses of 300,000 mouse units of a preparation of **follicular hormone**, followed by injections of a **luteal hormone**.

The menstruation was normal, in the sense that the mucous lining of the uterus curetted on the second or third day of bleeding showed all the histologic indications of a normal functioning endometrium on the twenty-eighth day of

the cycle. The ages of the patients were 25, 30 and 8 years, and they had previously never menstruated. The uteri of the 3 patients were hardly palpable and as a result of the treatment the uterus in each instance had increased in length to 5 and 7 cm respectively. On the first and seventh day, 1 c c (16 minims) of the follicular hormone (containing 100,000 mouse units) was given intramuscularly. On the fourteenth day another injection (50,000 mouse units), and from the twenty-second to the twenty-sixth day, 1 c c (16 minims) of corpus luteum hormone (10 rabbit units) was given. Menstruation occurred on the twenty-eighth day. The treatment also resulted in a development of the heretofore not strongly marked secondary sexual characters.

**ANTI-HORMONES.**—In the past year the question of “antihormones” has been discussed both from the editorial point of view (*J. A. M. A.* 103: 492 (Aug. 18) 1934) and by the experimentalists, H. Selye, J. B. Collip, and D. L. Thomson (*Proc. Soc. Exper. Biol. and Med.* 31: 487 (Jan.), 566 (Feb.) 1934); J. B. Collip (*J. Mount Sinai Hosp.* 1: 28 (May-June) 1934).

Selye and his associates have reported that injection of the anterior pituitary-like principle from the urine of pregnancy into rats over a sufficiently long time may lead to diminution in the size of the ovaries even to less than normal. When the ovarian-follicle-stimulating portion from the anterior pituitary gland was used by R. Hertz and F. L. Hisaw (*Am. J. Physiol.* 108: 1 (Apr.) 1934) in repeated injections into young rabbits, they found that at first the ovaries were enlarged 5-fold, but that they gradually regressed to their original size. Further injection of the extract did not elicit any ovarian response. The glands became refractory and after several months did not undergo normal development.

J. B. Collip and his co-workers have established the presence of definite antagonistic substances in the circulation (antihormones) by experimental means. The question of antihormones and their significance must be borne in mind when the treatment of an endocrinopathy is undertaken.

**DWARFISM, ENDOCRINE.**—The question of endocrine dwarfism and its treatment is discussed by William Engelbach and R. I. Schaefer (*J. A. M. A.* 103: 464 (Aug. 18) 1934). The problem of diagnosis and treatment of statural undergrowth or dwarfism rightfully belongs to the general practitioner and pediatrician. One has but to study the normal growth increment curve in the human being for this proof. It testifies to the fact that approximately 50 per cent of the total growth has been attained at the age of 3 years. Its increasing plateau diminishes rapidly as adolescence or sex maturity is attained. It logically follows that diagnosis and adequate treatment during the infantile and early juvenile periods should give the greatest therapeutic results.

There is an abundance of experimental evidence that the factor concerned in somatic growth is produced by the eosinophilic cell of the anterior lobe of the hypophysis. By this is meant that every structure of the body, from an individual cell to the constitutional whole, is involved.

The 3 postulates of hormonology, the therapeutic side of endocrinology, are completely fulfilled in the laboratory. This is demonstrated by the fact that immature animals are dwarfed by hypophysectomy. Adequate replacement

therapy in their instance will again bring about normal growth. An excess of this substance given to normal animals is capable of producing gigantism or acromegaly.

Engelbach and Schaefer reported the results of hormonal therapy in 7 cases of dwarfism. Injections of 2 c.c. ( $\frac{1}{2}$  dram) of an extract of beef **anterior pituitaries** were administered 3 times a week intramuscularly. No untoward results were noted at any time. The children were under a control period of from 2 to 6 months. Four cases have been under treatment continuously for over a period of from 14 to 15½ months. The increase in statural growth was from 3.3 to 6 inches. All of the patients received **thyroid extract** in therapeutic doses together with the growth substance, with the exception of 1 patient, who received the growth substance alone.

**HEADACHES, ENDOCRINE.**—Clinical experience and therapeutic results have convinced J. H. Sure (Wisconsin M. J. 33. 671 (Sept.) 1934) that certain headache syndromes are clinical entities, produced by abnormal functions of some of the endocrine glands, notably the ovary, the pituitary, the thyroid and the adrenals. While headache is frequently the outstanding symptom, there are many other manifestations of disturbed endocrine gland function.

The type of headache varies. It may be periodical, *i e*, pre- or postmenstrual, and is only occasionally continual. It may be hemicranial, temporal, parietal or occipital.

Sure proposes the following working classification of endocrine dysfunction (in the female):

- 1 *Hypergonadism*
  - (a) Hyperestrinemia (an excessive amount of sex hormone in the blood stream)
  - (b) Hyperprolanemia A (an excessive amount of anterior pituitary prolan A which activates the Graafian follicle)
- 2 *Hypogonadism*
  - (a) Hypoestrinemia (less than the normal amount of sex hormone in the blood stream)
  - (b) Hypoprolanemia A (lessened amount of Graafian follicle activator)
- 3 *Hyper- and hypoluteinemia* (an excessive or lessened amount of the products of the corpus luteum, progesterin, in the blood stream)
- 4 *Hyper- and hypoprolanemia B* (an excessive or lessened amount of the activators of the corpus luteum)
- 5 *Hyper- and hypothyroidism*
- 6 *Hyper- and hypopituitarism* (anterior or posterior)
- 7 *Hyper- and hypoadrenalism*

Sure gives a few case histories of patients in whom the headaches were associated with various menstrual abnormalities. By administering **theelin**, **pituitrin**, **antuitrin-S**, or **corpus luteum extract**, depending on the diagnosis of the endocrine gland suspected to be at fault, the headaches were generally ameliorated. The efficacy of treatment directed towards endocrine dysfunction will depend on the care with which the cases for treatment are selected.

**PITUITARY HEADACHE.**—The question of pituitary headache is described by W. M. Skipp (Endocrinology 18. 596 (Sept.-Oct.) 1934), who reports 11 personally observed cases of pituitary dysfunction with the charac-

teristic symptom of headache. During the end of the intermenstrual period the pituitary increases in size and causes the intracranial pressure to be increased. If the sella is smaller than normal, the pain is increased with hypertrophy of this gland. The hypertrophy may continue until the enlargement causes pressure on surrounding structures, with symptoms of optic nerve disease. According to Cushing, the pain is produced by increased intracapsular pressure of the pituitary.

The author obtained satisfactory results with the administration of **posterior pituitary lobe hormones** by mouth and subcutaneously. Extracts of the anterior pituitary lobe apparently were without benefit.

**MASTITIS, CHRONIC CYSTIC.**—In an analysis of 600 cases of chronic cystic mastitis, D. Lewis and C. F. Geschickter (*Am J Surg* 24: 280 (May) 1934) distinguish 2 types of the disease. In 1 there is a cystic formation, and in the other epithelial hyperplasia predominates (adenosis of the breast). The tendency of the cysts to vary in size and for the symptoms to be exaggerated in the premenstrual period is an expression of periodic variations of the secretory levels of theelin and progesterin. Frequently during pregnancy the lesions associated with chronic cystic mastitis disappear. The eventual disappearance of most of the undeveloped tubules and acini after repeated pregnancies explains the fact that chronic cystic mastitis is rarely met with in women who have borne children.

These observations likewise account for the frequent occurrence of cystic disease of the breast in married women who have not borne children and in the unmarried woman.

The authors believe that cystic changes in the apparently normal breast are due to variations in the amount of periodic discharge of the ovarian hormones (folliculin and progesterin). They arrive at this conclusion as a result of a study of the tissue in experimental animals after the injection of theelin, and theelin and progesterin combined, and of human material obtained at definite known periods of the menstrual cycle and pregnancy.

### **MENSTRUAL DISTURBANCES OF ENDOCRINE ORIGIN.**

**Treatment.**—Sufficient endocrine physiology is known to warrant a systematic study of menstrual disturbances which has for its purpose more exact diagnosis and specific treatment. C. A. Elden (*Am J Obst and Gynec* 28: 179 (Aug.) 1934) outlines the following course of study of patients to determine the glandular basis for menstrual disturbances. After a careful history relative to the endocrines is taken, a basal metabolism test is made, followed by a venipuncture for the determination of blood sugar, nonprotein nitrogen, urea, uric acid, and creatinine. Significant variations are shown in the high uric acid content of pituitary disease and the adrenal group, but in the latter the blood sugar is low. High residual nitrogen is also characteristic of the adrenal group. These findings are used in the differential diagnosis of endocrine disturbances after non-endocrine disease has been ruled out. Following the venipuncture, a galactose test is done. The estrin level is then determined on a 24-hour sample of fresh urine.

If the history, physical examination, and laboratory procedures seem to indicate disease of the pituitary gland, then accurate visual field, blind spot measurement, and stereoroentgenograms of the skull, centering on the pituitary fossa, are made.

By the method described, about 60 patients were studied for over periods varying from 6 months to 2 years. The author states that the response in several cases of *secondary amenorrhea due to hypopituitary function* to enteric-coated capsules of desiccated **anterior lobe of the pituitary gland** given in daily doses has been encouraging but not striking. It is believed that perhaps larger doses of the gland or a specific hormone-containing preparation would be of value in this type of case.

It is generally agreed that follicular hormone (**estrin, theelin, etc**) is useful in the treatment of *menopausal symptoms*. Elden has used it in his clinic in some few instances as an adjunct of the specific therapy, particularly in those cases where no estrin was demonstrable in the urine. He has not been able to initiate bleeding in a few of his cases of *amenorrhea* by means of apparently adequate doses of theelin. Encouraging results have been obtained with enteric-coated capsules of **anterior pituitary gland** in massive doses in cases of *functional uterine hemorrhage*. Until a gonad-stimulating preparation can be prepared from the gland itself, the use of pituitary-like preparations from the urine should be limited.

Elden has used **x-ray therapy** in some endocrine cases with favorable results, irradiation is applied only to the gland which seems to be primarily involved.

**Insulin** has been used successfully in the treatment of menstrual disturbances by H. Bultemann (Zentralbl f Gynak 52. 1841, 1928). Its use is not without basis, since an occasional correction of amenorrhea has been noted in the treatment of diabetes mellitus with insulin.

**Cortin** may be used in cases of *adrenal insufficiency* in women with secondary amenorrhea, menstruation having returned under this treatment.

**OVARY.—TUMORS OF.**—A very interesting case of *precocious sexual development* in a 7-year-old child has been described by P. B. Bland and Leopold Goldstein (Am J Obst and Gynec 28 596 (Oct) 1934). The premature development of sexual characteristics and the onset of menstruation were caused by the endocrine activity of recurrent *granulosa cell tumors of the ovary*. The estrin pregnancy test was positive 2 days prior to operation. Up to the present time 7 cases of granulosa cell tumor of the ovary, all associated with the clinical syndrome of precocious puberty, have been recorded.

**Operative removal** of the tumor usually brings about a cure. In view of the number of cases reported in which recurrence has taken place, it is recommended that **postoperative radiotherapy** be administered.

**PINEAL BODY.—Physiology.**—Clinical observations in patients with tumors of the pineal body led William Saphir (Endocrinology 18 625 (Sept-Oct) 1934) to study experimentally the function of the gland. Patients with pineal body neoplasms usually offered the most impressive picture of precocious

puberty or macrogenitosomia precox. The interpretation of the symptoms of precocious puberty found in cases of pineal growths was based upon the assumption of either an *hypopinealism*, due to destruction of pineal tissue by the tumor, or an *hyperpinealism*, due to stimulating effect of the tumor upon the glandular secretion.

In view of the many contradictory experimental findings, the author undertook to study the action of the human pineal gland upon the sexual cycle of (adult) female white mice by the method of implantation. Human pineal bodies were implanted intramuscularly into the thigh of 5 female mice and vaginal smears were examined later which did not show any variation from the normal. The experiment was repeated, employing castrated mice. Estrin was produced after a period varying from 5 to 8 days. In no instance did implantation of several pieces of human pineal gland into infantile mice result in ovarian stimulation.

The experiments seem to indicate that the human pineal body exerts an estrogenic influence upon the castrated mouse. The theory is offered that the clinical picture of *pubertas precox* in cases of pineal tumors results from an increased glandular secretion due to the active stimulating effect of the tumor. On the other hand, the fact that in certain pineal tumors no trace of pineal tissue remains has given origin to the view that the normal pineal gland produces an inhibiting influence upon sexual development and that lack of this inhibiting influence, due to destruction of the organ, leads to precocious puberty. Therefore, a definite decision in favor of one or the other theory becomes exceedingly difficult to make.

#### PITUITARY GLAND.—HYPOPITUITARISM IN MALE.—

**Treatment**—Since many of the endocrine disturbances arise in infancy or early childhood, a great responsibility falls upon the pediatrician for their early diagnosis and treatment. The early recognition of hypophyseal deficiency or dysfunction might prevent the unhappy state of dwarfism, sexual infantilism, various menstrual disorders, certain cases of sterility, obesity, etc., in later life. In a study of hypopituitarism in the male, R. H. Kunstadter and I. S. Robins (J. Pediat. 4: 774 (June) 1934) undertook the management of this condition with endocrine therapy.

In this study, 8 male children were selected, their ages ranged from 5½ years to 15½ years at the onset of treatment. All were diagnosed hypopituitarism by means of their clinical features and laboratory data. The treatment consisted of the hypodermic administration of **anterior pituitary-like sex hormone**, 3 times weekly, in the dose of 100 rat units, for periods of 3 to 6 months. In 1 case this therapy was complemented by the oral administration of desiccated **anterior lobe pituitary**.

In all cases weights and complete measurements were recorded at frequent intervals and particular notice was taken of appearance of the secondary sex characteristics, genital growth, and fat distribution. Five of the patients received a complete blood count, urinalysis, blood chemistry, including nonprotein nitro-



gen, cholesterol and sugar tolerance determination, basal metabolism, and x-ray of the sella turcica.

*Results of the treatment* were as follows: Descent of the testes was accomplished in all 3 cases of *cryptorchism*. In 3 cases characterized by genital underdevelopment (*testes descended*), treatment resulted in enlargement of the testes and scrotum and the appearance of the secondary sex characteristics. In 2 cases characterized by *pituitary obesity* with normal genital development, treatment resulted in no increase in the size of the genitals. In 4 of 5 cases receiving basal metabolism tests before and at the end of treatment, the basal metabolic rates were lowered below the lower limits of normal at the end of treatment. In 7 of the 8 cases, there was an increase in *growth of stature* above the normal for the age following treatment. In their series of cases, prolan (anterior pituitary-like sex hormone) did not stimulate weight loss and did not alter the typical pituitary distribution of fat.

An interesting case of so-called functional hypopituitarism in a man aged 35 years, is described by D. A. De Santo (Arch. Neurol. and Psychiat 31 134 (Jan) 1934). The patient gave a 10-year history of progressive adiposity reaching 450 lbs (204.5 kg.), with later development of headache, polyuria, somnolence, hypertension, exophthalmos and genital atrophy. These symptoms were attributed to a cyst-like destruction of the posterior lobe of the pituitary gland found at necropsy, with the exception of the testicular atrophy which was probably related to a small area of sclerosis in the anterior lobe. No gross deformity or lesions were discernible in the region of the third ventricle. It is believed that the pituitary gland is not infrequently modified by acute and chronic infections, sufficient to cause pituitary disorder.

**PITUITARY BASOPHILISM.—Clinical Types.**—According to I. H. Pardee (Arch. Neurol. and Psychiat 31 1007 (May) 1934), there are 5 syndromes of pituitary basophilism: (1) the Cushing syndrome, (2) a mixed syndrome of intrasellar pituitary disease; (3) a syndrome in which the disturbances appear to point to involvement of the suprarenal cortex, (4) a prepubertal or pubertal basophilic syndrome, and (5) the postmenopausal basophilic syndrome. The author attempts to demonstrate that not all basophilic syndromes are necessarily progressive and fatal. Likewise, he endeavors to point out that pituitary adenomas presenting many features of this syndrome exist, and are either purely pituitary basophilism or combined with acidophilism and disease of the adrenals, also, that "transitory or mild degrees of pituitary basophilism" (Cushing) do exist, not only in adolescents, but in premenopausal and postmenopausal states.

Pituitary basophilism, as described by Cushing, is characterized by a rapidly acquired obesity, which affects chiefly the face, neck, and trunk; hypertension, decalcification of bones of the skeleton, and purplish striae of the abdomen are additional special features of the disease. Several cases of this endocrine condition have been reported in detail during the past year.

**CASE REPORTS.**—A report of a case of pituitary basophilism occurring in an unmarried woman, age 23 years, has been placed on record by M. G. Wohl and his associates (Radiology 24 53 (Jan) 1935). Her chief complaint was pain in the lower third of the right tibia and

right foot and ankle, and rapid gain in weight. She was also bothered with swelling of both ankles, which was of 9 months' duration, and always worse toward evening.

During the past year she had developed shortness of breath, a growth of fine hair on the upper lip and the under-surface of the chin, and on 2 occasions dizzy spells that lasted 3 days. She noticed a steady, progressive gain in weight, having gained 25 pounds in the past 9 months.

Her menses commenced at the age of 12, lasting 7 days, and were accompanied by considerable dysmenorrhea. In the past 14 months the menstrual flow had become scant and the periods irregular. Physical examination showed an obese, sluggish young woman, 5 feet 4 inches in height and 232 pounds in weight. The face was round and the site of an old acne, with considerable scarring and pitting. There was a thin growth of hair on her upper lip and chin. The breasts were pendulous. The skin was dry and there was a growth of hair from the symphysis pubis to the navel. On both lateral and anterior aspects of the lower half of the abdomen prominent purplish striae were present.

Examination of the heart and lungs revealed no abnormalities. The blood-pressure varied from 155/85 to 140/90. Examination of the visual fields revealed a sector-like constriction in the right upper temporal field and slight constriction in the left upper temporal quadrant. The fundi and media were normal.

The basal metabolic rate was minus 26 per cent. She had a high tolerance for carbohydrates. Oral administration of 100 Gm (3½ ounces) of glucose caused a rise in blood sugar in 1 hour to 114 mg per 100 cc of blood, but this figure dropped to 105 mg at the end of the third hour. The blood cholesterol was 180 mg per cent. The blood calcium was 11.5 mg per cent, and blood phosphates 4 mg per cent. The urine contained a trace of albumin.

X-ray examination of the right foot showed areas of rarefaction in the metatarsal bones and phalanges. X-ray examination of the right leg showed similar areas of rarefaction in the tibia. The sella turcica was entirely normal in size and shape.

The patient was placed on a **restricted diet** of 1500 calories, and on **thyroid medication**. She was given a series of **x-ray treatments**, 250 R to each side of the cranium at the first visit and 100 R at weekly intervals thereafter, until 6 treatments had been given in all. The exact position of the sella turcica was determined by x-ray examination and fluoroscopy of the skull.

Her general condition promptly improved—the blood-pressure decreased, the pain in the right lower extremity markedly diminished, her weight rapidly declined to 215 pounds. X-ray pictures of the right foot and right leg, made 2 months after the completion of the series of x-ray treatments, showed that the areas of rarefaction had become much smaller, due to filling in of new bone. A recent x-ray examination of the right foot and leg (11 months after the original examination and 9 months after the x-ray treatments to the pituitary) shows scarcely any defects in the bones. Her menstruation became regular and of normal flow.

Without a postmortem verification it is hazardous to state which gland was chiefly responsible for the endocrinological signs. However, the fact that irradiation of the pituitary gland brought about not only calcification of the osteoporotic bones, but also improved the patient's general condition, would favor the conclusion that the pituitary gland played the primary rôle in the patient's condition.

A case of basophil adenoma of the pituitary body is described by John Craig and Brennan Cran (*Quart J Med* 3 57 (Jan.) 1934), which was diagnosed during life and confirmed by autopsy.

The patient, a female aged 28, single, was seen first on August 25, 1932. About 4 years previously she began to get stout about the abdomen and chest, and soon after the upper arms and thighs also became enlarged. Some months before the onset of the obesity, hair began to grow on her chin, and during the 4 years of her illness, the hair on the face and lips increased, as also did the hair on her limbs. The menstrual periods had always been

regular, and normal, but from the onset of the illness they became irregular—usually coming at 3-monthly intervals. In April, 1932, they ceased altogether.

For 2 years she had occasional frontal headaches, especially in the mornings. For 18 months increasing breathlessness was complained of, and she had several attacks of acute dyspnea during the last few months. From the onset of the illness she had become increasingly highly colored, and had noticed an increase in the pigmentation about her face. In the last year she had rheumatic-like pains in her arms and legs.

*Examination*—Patient was a plethoric woman who weighed 217 pounds and was 5 feet 4 inches in height.



A

B

C

(A) Photograph before onset of disease (B) Showing adiposity and general appearance and abdominal striæ (C) Showing peculiar condition of lower legs (Craig and Cran Quart J Med)

There was diffuse brown pigmentation about the face, which was rather obscured by her blue color. There was a well-marked growth of hair on the chin, the upper lip, and the lower cheeks. There was some dark hair on the back of her hands and forearms, and on the shoulders and thighs. The upper arms and thighs were larger than normal from deposition of fat. The arms generally were rather blue, the blueness being most marked about the hands and wrists. There were many dark brown pigmented spots on the tibial surfaces of both legs, as well as some transverse striæ and a few ecchymoses. There was slight edema about the ankles. Fatty masses were found over the lower cervical vertebræ, and were also present on each thigh continuous to the labia. The breasts were large, fatty, pendulous, and showed a bluish tinge, some dark brown pigmented spots, and a few striæ. The trunk generally was obese and the abdomen corpulent and protuberant. The abdomen was covered with large striæ, some purple and some pale, and obviously of different dates. The hair on the abdomen had a masculine distribution. The skin was moist.

The blood-pressure was elevated. In the right arm the pressure was 180/118, and in the left arm 178/116. No tumors could be felt in the abdomen. The lungs were normal. The urine contained a faint trace of albumin. The blood urea was 23 mg per cent. The blood count showed 110 per cent hemoglobin, 6,190,000 red cells, and 7400 white cells, of which 64 per cent were polymorphonuclears.

The serum calcium was 10.8 mg per cent, and the plasma phosphates were 2.01 mg. per cent. A sugar tolerance test was done, and showed the following blood-sugar values after the ingestion of 50 grams of glucose:

Fasting blood-sugar	.. . . .	0.092 per cent
Half-hour	.. . . .	0.104 per cent
One hour	. . . . .	0.109 per cent
One and one-half hours	. . . . .	0.133 per cent
Two hours	. . . . .	0.109 per cent

Nothing abnormal was found generally in the nervous system. The fields of vision were full. Visual acuity was good.

The Wassermann reaction of the blood was negative. Radiograms showed general decalcification of all the bones of the body. The sella turcica measured 16 mm. antero-posteriorly and 10 mm. in depth.

On vaginal examination, the pelvic organs were found to be normal. The urinary tracts were visualized by uroselectan B and the radiograms showed the pelvis and ureters to be normal in shape and position.

The case was clinically diagnosed as a basophil adenoma of the pituitary gland. Accordingly, deep **x-ray therapy** was applied to the pituitary gland, and exposures were given over 5 areas, *i e*, frontal, vertical, occipital, right temporal, and left temporal. She returned for a second course in December, 1932, and was then found to have a suppurative prepatellar bursitis. While in the hospital she developed a common cold, which led in a few days to a purulent pneumococcal bronchitis, and she died January 7, 1933, with a right-sided empyema.

At autopsy, a basophil adenoma of the anterior pituitary lobe was found. Section of the pituitary gland showed that its enlargement was due to the presence of a soft, pale yellow, oval tumor, which was situated chiefly in the right half of the anterior lobe. The pituitary fossa appeared normal, and the clinoid processes were unaltered.

**Diagnosis.**—Two cases have been described in which a basophil adenoma of the pituitary was suspected at autopsy on account of the physical appearance of the subjects and the presence of a conspicuous degree of cardiovascular hypertrophy, *D. S. Russell, Horace Evans, and A. C. Crooke (Lancet 2:240 (Aug. 4) 1934)*. The possibility of a pituitary adenoma had been considered at an early stage of the illness on account of severe headache, obesity and impotence (male), but was discarded when the x-ray examination proved to be negative. Later the case was regarded as one of essential hypertension. In retrospect several of the principal clinical features of Cushing's disease could be identified in this case, *i e*, the obesity of peculiar distribution associated with abdominal striae, hypertension, plethora, skin hemorrhages and impaired sexual function. Certain changes claimed as part of the syndrome were lacking—namely, osteoporosis and skeletal deformities, glycosuria and hypertrichosis.

In the second case, repeated albuminuria of pregnancy was associated, at least in the last pregnancy, with raised blood-pressure without nitrogen retention. Cardiovascular hypertension, obesity and a moderate degree of hypertrichosis were the only physical features that could be associated with pituitary adenoma.

In the pituitary alone of the endocrine organs was there an abnormality common to both cases?

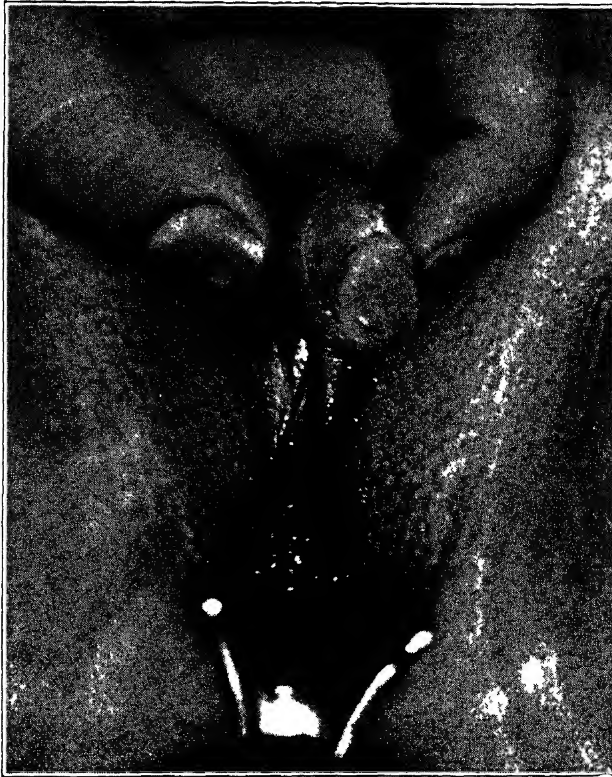
In a recent paper, Cushing suggests that basophilic invasion of the posterior lobe may be potent in producing the features of this syndrome as well as the clinical conditions of eclampsia and essential hypertension. He was led into putting forward this suggestion by finding, in addition to a basophilic adenoma,

an extensive infiltration of the posterior lobe with basophil cells in a fatal case of his syndrome.

**PSEUDOHERMAPHRODITISM.**—This condition has always been a subject of interest to the urologist, gynecologist and general practitioner. A very interesting case report has recently been published by R. S. Finkler (J. A. M. A. 102:924 (Mar. 24) 1934).

**CASE REPORT**—The patient, brought up as a girl, was first seen 5 years ago at which time she was 13½ years old. She was short and stocky, very timid, and had a deep masculine voice, a square masculine chest without any signs of breast development, and a masculine distribution of hair on the body and extremities. Menstruation had not yet begun.

When the child was 14 years of age, the mother discovered an appendage at the site of the clitoris. On examination the appendage appeared to be an imperforate penis about 5 cm. long. On voiding, the urine seemed to come from the vagina. Rectal examination revealed a small, hard uterine body lying anteriorly, no ovaries could be palpated.



Penis shown in place of clitoris. Vagina brought into view by the use of a speculum (R. S. Finkler J. A. M. A.)

Five weekly specimens of blood were taken and examined for the presence of estrin by the Frank-Goldberger method. The fourth specimen showed a trace of the hormone.

An exploratory section was performed which disclosed an underdeveloped uterus and tubes and ovaries. A careful search failed to reveal the presence of testicles. Palpation of the adrenal glands did not reveal the presence of a tumor. Because the pelvic organs were those of a female, the hypertrophied clitoris was removed. She was placed on endocrine therapy which was checked by hormone studies of the blood and urine. Blood studies never showed more than a trace of estrogenic substance, but the urine showed a rapid elimination of both hormones.

After *treatment* over a period of 1 year there was some improvement in the physical and psychologic make-up of the patient. The voice began to lose its masculine tone, and she became less timid and silent. However, she did not begin to menstruate. Hair continued to grow on her face. An aqueous preparation of the **anterior pituitary lobe** prepared by the Van Dyke and Wallen-Lawrence Method was obtained and used in conjunction with filtered pregnancy urine. Five c.c. of urine of pregnancy and 1 c.c. of the growth-inducing preparation were given intramuscularly every other day. Small doses of **desiccated thyroid** were given at intervals. On March 16, 1933, after about 10 weeks of treatment, when the patient was 18½ years of age, her first menses appeared, which lasted 7 days. At this time the hairy growth on her face began to diminish. She has had several additional periods at intervals of 4 to 5 weeks. Her features and body are rounding out, the breasts are beginning to develop, and the voice is almost entirely feminine in character.

**PREGNANCY.—HORMONES IN TOXEMIA.**—Recently, G. V. Smith and O. W. Smith (Am J. Physiol 107 128 (Jan.) 1934) have shown that the blood and urine of toxemic patients in late gestation contain a much larger amount of the anterior pituitary-like substance (prolan) than ordinarily occurs in pregnancy. These writers have demonstrated that a quantitative imbalance between prolan and estrin is characteristic of the toxemias of late pregnancy. In 12 pregnant women without symptoms there were, on the average, 50 rat units of prolan per 100 c.c. of blood serum, while 18 toxemic patients showed 250 units and 5 eclamptics showed 480 units. The amounts of estrin (female sex hormone, follicular hormone) were correspondingly reduced.

**SEXUAL UNDERDEVELOPMENT.—Treatment.**—The effect of the anterior pituitary-like hormone of urine of pregnancy in the development of the male genitalia is discussed by D. L. Sexton (Endocrinology 18 47 (Jan.-Feb.) 1934). Experimentally, the works by Lower and Johnson, Engle, Riddle and others have shown conclusively that this hormone is capable of stimulating the development of the sexual organs.

The author reports on 13 boys who exhibited genital underdevelopment among their chief complaints. Their ages ranged from 10 to 21 years. The striking points in the physical examination were genital aplasia and statual underdevelopment, showing a lack of both the gonad-stimulating and the growth-promoting hormones of the anterior pituitary. X-ray studies revealed a marked delay in closure of the epiphyseal centers, a finding long associated with advanced hypopituitarism.

The patients were treated with intramuscular injections of the **anterior pituitary-like hormone of pregnancy urine**. Eleven of the subjects responded to treatment by an increase in the size of the external genitalia and the appearance of secondary sex characteristics. These 11 were obese, while the 2 who failed to respond were thin. Cryptorchism was present in 6 of the 13 cases, and in 4 of these 6 the testicles localized in the scrotum after treatment.

The dosage and duration of treatment was dependent on the degree of underdevelopment and the age. Those in early adolescence responding most favorably

**THYMIC ENLARGEMENT.**—Questions frequently arise concerning the routine use of x-ray therapy of the chest before operation for an enlarged

thymus in children. There has been a decided change of opinion on this question in recent years. Enlargement of the thymus, either alone or in conjunction with a generalized adenopathy, was considered a usual cause of sudden death in infants and young children. During the past 2 years the attitude has been expressed that enlargement of the thymus should never be credited as causing these sudden deaths. Of the more recent contributions tending to explain sudden death associated with enlargement of the thymus, G. L. Waldbott (Am. J. Dis. Child. 47:41 (Jan.) 1934) reports the pathologic process in 34 cases and discusses the observations and their explanation from an anaphylactic standpoint. He feels that allergic studies should be made in all cases in which there is x-ray evidence of an enlarged thymus.

At present it is not customary to make x-ray examinations of the chests of all children with enlargement of the thymus before operation. Infants under 1 year of age are usually examined with the fluoroscope or the x-ray if time permits, and always in the event of any symptoms.

It is probably advantageous to examine the chests of all infants with the fluoroscope, whether or not operation is contemplated.

With proper precautions and in competent hands, the exposure to x-rays necessary to produce shrinking of an enlarged thymus is accompanied by a minimum risk.

**STATUS THYMICOLYMPHATICUS.—Pathogenesis.**—The subject of *status thymicolymphaticus* is summarized by M. Szabados (J. Pediat. 4:798 (June) 1934) who finds, from a review of the literature, that in this condition asphyxia is not symptomatic, but causative.

The hypothesis is advanced that the *rôle of the thyroid* in *status thymicolymphaticus* is compensatory to a primary asphyxial cause. The different causative factors which are known to stimulate the thyroid all merge into one principle, that of primary asphyxia, which is antecedent to the rise of basal metabolism. The statement that the stimulation of the thyroid is compensatory for asphyxia may be made because some form of asphyxia was uncovered in all thymicolymphatic states as the only common characteristic which can account for the thyroid stimulation, essential for all these conditions, and because thyroid stimulation is always secondary to asphyxia. Continued increase of basal metabolism is considered as the result of overcompensation.

The generalization that asphyxia is the only cause of thyroid stimulation is contrasted with the opinion that has been expressed that asphyxia is one of the causes of thyroid stimulation in thyroid crises and Graves' disease. This generalization became possible through the recognition that increase of adrenalin liberation was reported in all conditions which are stated to produce thyroid crises and Graves' disease. Increased liberation of adrenalin was taken as an indicator of a state of asphyxia. In Schmorl's statistics, extending to 517 cases of varied pathologic conditions, increased production of adrenalin was found only in those characterized by asphyxia. Increased liberation of adrenalin and asphyxia appear to denote the same thing in medicine. Cannon's discovery that asphyxia stimulates the adrenalin output appears to have a universal significance.

The asphyxia hypothesis was applied to all clinical syndromes of status thymicolymphaticus, and to the experimental production of thymicolymphatic overgrowth by removal of the suprarenal cortex, which appears to be one of the numerous ways by which asphyxia may originate.

The validity of the asphyxia hypothesis was further tested by its application to the *sudden death* problem. This basic requirement could also be satisfied. The pathologic findings in sudden death in status lymphaticus are seldom sufficient to explain death. A mechanism of death which does not leave sufficient trace, *viz*, ventricular fibrillation, is considered to be the cause by Aschoff. This mechanism is consistent with the increased liberation of adrenalin in asphyxial states. Increased adrenalin content of the suprarenals was found in 2 cases of sudden death by Schmorl. The effect of increased adrenalin in sudden death may further be inferred from the hyperpyrexia of the body described by Aschoff and from the more or less marked pulmonary edema.

Thus, there is an all-including hypothesis of status thymicolymphaticus which has no exceptions and offers a satisfactory explanation as to the rôle of the thyroid gland in these conditions. It also explains satisfactorily the original problem of sudden death. The search for a solution for this enigmatic phenomenon led Paltauf to the discovery of status lymphaticus.

**THYROID.—HYPERTHYROIDISM.—Treatment.**—The treatment of hyperthyroidism by **irradiation** is presented by J. W. Cathcart (Southwestern M. J. 18:191 (June) 1934). Suitable for irradiation (x-ray or radium) are all forms of toxic goiter in which the tumor is not producing marked pressure symptoms, also any case where surgery is contraindicated by reason of an intercurrent disease, such as diabetes, heart disease, etc.

Irradiation therapy of hyperthyroidism is free from many of the objections to surgery. The mortality is zero. There is no question of safe anesthetic, no detailed technique which may go wrong and injure the recurrent laryngeal nerve or the parathyroids, no air embolism, no acidosis, no postoperative toxic crisis.

Irradiated patients are seldom hospitalized and in most instances continue with their usual occupations, giving only added special attention to rest and diet.

There is no danger to the parathyroids, and myxedema very seldom follows irradiation. The length of time required for treatment by irradiation is used as an argument in favor of surgery, but this is not as great as it might seem. The average surgical preparation takes about 2 weeks and allowing 2 weeks for the operation and 30 days for convalescence, 2 months have been used. During that same time a patient being treated by irradiation should show a marked improvement, although he will still be under treatment.

The question of injury to the heart through delay by patients first trying irradiation seems not to be well founded. On the contrary, there are many eminent surgeons who advise irradiation to prepare their worst cases for operation. There are others who believe irradiation to be suitable for cases with a basal metabolic rate below 40.

G. E. Pfahler (Radiology 18:879 (May) 1932), by correspondence with 8 of the outstanding radiologists of this country, traced the results in over 1200



cases of toxic adenoma that had been treated by irradiation, and found not one in which malignant degeneration subsequently took place. He therefore concluded, "since carcinoma of the thyroid seems to be especially sensitive to irradiation, we may in fact be preventing or curing such early degeneration."

Cathcart employed **x-rays** and **radium** interchangeably, considering them of equal value. Radium has been used principally in highly toxic cases with fibrillation to such an extent that the patients were confined to bed in their homes or in a hospital. The radium technic consists of blocking-off the thyroid and applying 100 mg., heavily screened, at a distance of 3 cm. Fifteen hundred mg. hr. are given at a treatment; the second treatment is given in 2 weeks, and after that every third week.

The x-ray technic consists of 140 K. V. 5 milliamperes, 12 minutes, filtered through 4 mm. of aluminum, at a distance of 38 cm. This treatment is given through each of 2 semilateral parts and extends down over the thymus area, as it has been shown that the thymus is frequently enlarged in goiter cases. The same interval is used as in radium treatments. Neither of the technics described will produce structural changes in the tissue that will in any way interfere with a subsequent operation, should it be deemed advisable.

Irradiation acts on the gland by first reducing the secretion of thyrotoxin; later, this is followed by a shrinkage in the tumor. The thyrotoxicosis disappears more rapidly than the goiter.

Iodine in the form of **Lugol's solution**, 5 to 10 drops in milk, 3 times a day, or **quinine hydrobromide**, 5 grains (0.3 Gm.) 3 times daily, is used as an adjuvant during the early weeks of the series of treatments, but is discontinued as the basal metabolic rate approaches normal, thus leaving to irradiation to establish the normal amount of secretion to be retained.

The average metabolic rate at the beginning of treatment was plus 31.5 and at the completion of treatment, minus 1.2. The average gain in weight was 8 pounds. The average number of treatments given in the series of 83 cases per patient, was 7.

I. Bram (M. Rec. 140.67 (July 18) 1934) reports his observations with **adrenal cortex** in the treatment of Graves' disease based upon studies on 12 cases. He used a glycerinated extract of the cortical substance in the form of 10-gram (0.6 Gm.) pills given in doses of 3 or 4 pills, 3 times a day. Smaller doses were inadequate. Twelve patients treated without adrenal cortex were observed as controls. Both groups were kept under a broad régime of medical attention including a **modified rest** program, an **ample dietary**, and **psychotherapy**. Also, both groups received the necessary sedatives and other indicated medicaments. The object of this study was to note whether favorable progress occurred more speedily in those receiving adrenal cortex.

Adrenal cortex therapy is harmless in all cases and presents a varying degree of usefulness in many. His observation indicates that it is of considerable value in the type of syndrome presenting the following clinical features: little or no thyroid swelling, little or no exophthalmos; arterial hypertension, moderate loss in weight, a rather stubborn tachycardia, the heart rate reaching 130 to 160 per minute, and the basal metabolic rate varying between plus 40 and plus 70 per

cent. The average age of these patients is 32, and the sex incidence is approximately 1 male to 3 females. While this type yields rather tardily to the usual therapeutic remedies, the patients respond rather promptly when glycerinated adrenal cortex is included in the régime.

In the 12 cases under the clinician's observation it was found that the inclusion in treatment of adrenal cortex resulted in comparatively prompt relief from tachycardia, the heightened basal metabolic rate, the nervousness and fatigability. This relief occurred approximately 8 weeks sooner than in the control patients. The average duration of the administration of adrenal cortex was 10 weeks.

**UTERINE HEMORRHAGE, FUNCTIONAL.**—Leopold Goldstein (Internat. Clin. 3. 135 (Sept.) 1934) discusses at length the problem of idiopathic or functional uterine hemorrhage.

Functional menorrhagia may assume one or more of several different forms, ranging from merely prolonged and profuse flows at irregular intervals to almost continuous oozing. Mild cases are seen in patients who have had a 28- or 30-day cycle, but in whom the bleeding period has become profuse or prolonged as compared with preceding menses. In other patients, the onset of the menses may be delayed and the bleeding period may last 2 to 4 weeks or longer. In some individuals the bleeding may be almost continuous for several months, interrupted only by short sessions free from bleeding. In others, continuous hemorrhage sets in after an amenorrheic period of several months.

It must be remembered that the diagnosis of essential or functional uterine hemorrhage precludes the presence of gross organic pelvic disease (newgrowths, inflammatory conditions, etc.) as well as general conditions giving rise to uterine bleeding, such as the various blood dyscrasias (leukemia, purpura, thrombocytopenia), lues, etc.

**Treatment.**—**HORMONAL THERAPY.**—From the physiologic standpoint, **progestin** (extract of corpus luteum) should be the ideal agent in the therapy of functional uterine bleeding. The rationale of the treatment has been indicated by the experimental investigation of P. E. Smith and F. T. Engle, in which uterine bleeding in the *Macacus* monkey was prevented by injections of corpus luteum extract. It is now known that in the spayed or immature monkey uterine bleeding from an interval type of endometrium occurs about 6 days after cessation of sufficient treatment with estrin (Allen, Maddux, Moriell). Uterine bleeding is also known to take place from an interval type of endometrium in the intact normal monkey injected with extract of pregnancy urine (Engle). Smith injected anterior pituitary sex hormone derived from sheep pituitaries into the adult *Macacus* monkey for 10 to 14 days. Simultaneously with the last 4 of these injections, estrin was given (100 rat units per day) and bilateral ovariectomy was performed which, alone, is followed by uterine bleeding. On the day ovariectomy was performed, treatment with progestin was started. Bleeding never occurred during the course of this treatment, and was prevented in various animals for periods of 10 to 28 days after the double stimulus to bleeding afforded by the bilateral oophorectomy and the cessation of estrin therapy.

If potent extracts of corpus luteum were available, it should be possible to nullify the effect of estrin on the endometrium and transform the hyperplastic endometrium into a secretory progestational type, with probable completion of the cycle and cessation of hemorrhage. In the absence of a potent **corpus luteum** preparation, the administration of the luteinizing hormone of the **anterior pituitary** (which would convert the granulosa cells of the ovary into lutein cells that, in turn, would manufacture progesterin) offers the best therapeutic procedure. The progesterin would transform the stationary hyperplastic endometrium into a pregravid one, thus arresting the bleeding.

The mechanism by which the bleeding is terminated is not clear. It may be brought about either through the primary action of the anterior pituitary sex hormone on the persistent Graafian follicle, or through stimulation of an existing defective or functionally inactive corpus luteum which had been responsible for the bleeding.

The author has found the employment of large doses of luteinizing hormone of **anterior pituitary** (100 to 200 rat units daily, hypodermically) of great value in the treatment of functional uterine hemorrhage during any period of the reproductive life. Occasionally, a single dose of the preparation brings about complete cessation of the bleeding.

It may be stated here that preparations of anterior pituitary sex hormone are of no value in preclimacteric cases. Here, as previously mentioned, there usually exists a compensatory hyperfunction of the anterior hypophysis, expressed by an excess of the pituitary sex hormone in the circulating blood (positive Fluhmann test), and the administration of additional amounts can, therefore, be of no benefit.

In the hormonal treatment of functional uterine hemorrhage, 2 points must be borne in mind. (1) The treatment must be continued until a normal flow occurs, as merely extending treatment until bleeding ceases does not suffice (2) Large doses are required, 100 to 200 rat units to be given every other day until a normal flow occurs.

Twenty-one cases of functional uterine hemorrhage in women under 40 years of age were treated by the writer with preparations of luteinizing sex hormone made from the urine of pregnancy (**prolan**). The products contain a hormonal substance similar to (if not identical with) the sex hormone of the anterior pituitary lobe. Three patients were pubescent girls, the remaining 18 were mature women.

Sixteen patients received injections of either follutein or antuitrin-S (in doses of 100 to 200 rat units every other day), while 5 received injections of whole urine of pregnancy, 20 c c every other day. Uniformly good results were obtained by the procedure outlined above. Sixteen women were entirely cured of their menorrhagia and the other 5 showed decided improvement.

The following case is illustrative of the value of hormonal therapy in the obstinate menorrhagia of maturity:

A nulliparous woman, aged 25, moderately obese (height, 5 feet 3 inches; weight, 170 pounds—77 kg.), came under observation in October, 1932. Her menses had commenced at the age of 14, recurring every 4 weeks and lasting 7 to 10 days. At 17 years she had a period

of amenorrhea of 4 months, followed by a return of regular menses of 7 days' duration every 28 days, for several months. In 1930, amenorrhea recurred for a period of 2 months. Later, in January, 1932, after a menstrual flow lasting 8 weeks, she underwent a curettage. This gave no relief, however, and 6 months later the measure was repeated.

The basal metabolic rate on 2 occasions was normal. There was no hypertrichosis nor any other stigma of endocrinopathy. The visual fields were normal and pelvic examination disclosed no abnormality.

When first seen, she had been bleeding for 3 weeks. Daily injections of 2 c c ( $\frac{1}{2}$  dram) of **antuitrin-S** were given for 5 days, with decided improvement within 3 days of the beginning of therapy. Treatment was continued in smaller doses (100 rat units) repeated every other day until bleeding ceased entirely. After a period of amenorrhea of 8 weeks she had a menstrual flow, which promised to last longer than 7 days, and the treatment was, therefore, renewed. Two doses of antuitrin-S (200 units per dose) on successive days was sufficient to halt the menstrual flow at this time.

Recent experimental investigation by Evans and his co-workers has shown that a combination of **prolan** (gonad-stimulating substance from the urine of pregnancy) and the purified growth fraction of the **anterior pituitary lobe** produces a marked stimulative effect on the ovary, far greater than could be obtained by the administration of either component alone. These findings at once suggest the employment of prolan in combination with nonsexual pituitary growth hormone in the menstrual disturbance under discussion, but it is still too early to make any general statement regarding results to be expected from this therapy.

The endometrial hyperplasia giving rise to abnormal uterine bleeding is occasionally so extreme (polypoid formation) that hormonal treatment is ineffective without a preliminary removal of the pathologic tissue. Injections of prolan (lutemizing hormone from urine of pregnancy) will, however, prevent the otherwise inevitable recurrence of the condition.

Campbell and Collip have found that treatment with an **extract** derived from the **placenta**, decidedly similar to anterior pituitary, is of considerable benefit in menorrhagia and metrorrhagia. In simple types of menorrhagia, the administration of this extract for 1 week before the epoch materially reduced the flow in a number of patients.

**Thyroid extract** is of remarkable value, especially in functional menorrhagia of adolescence. Of 7 patients with severe menorrhagia, Plass states that the results secured by cautious use of thyroid extract are so good as to suggest administration of the drug to such patients even in the absence of a low metabolic rate.

That **parathyroid extract** may also be beneficial in controlling excessive menstrual bleeding is shown by Allen and Goldthorpe, who obtained good results in 5, fair results in 6, and poor results in 3 cases of severe menorrhagia. The optimum seem to be about 40 units given intramuscularly each day over a period of 5 days. Best results are obtained when the hormone is combined with 120 to 180 grains (8 to 12 Gm.) of a **calcium** preparation.

**RADIOTHERAPY**—In a recent analysis of 423 cases of functional uterine bleeding, treated at the University of Pennsylvania Hospital during the 10-year period ending 1931, Keene and Payne found that **radium therapy** (200 to 500 mg. hrs.) in women up to 30 years of age restored menstruation to normal or

nearly normal in 88 per cent. Permanent amenorrhea, however, developed in 6 per cent, and severe menopausal symptoms in 8 per cent. Although the bleeding was controlled by radium therapy in 95 per cent. of the patients between 30 and 40 years of age, permanent amenorrhea developed in 24 per cent. and severe menopausal symptoms in 21 per cent. These patients had received dosages of radium varying from 200 to 1200 mg. hrs. These authors believe that, with a reduction of the initial dosage to 300 mg. hrs and an increase of not more than 100 mg. hrs in case re-radiation becomes necessary, radium therapy is the method of choice in patients of this age-group. The excellent results reported by various competent observers with the use of prolan render the use of radium with its attendant ill effects unnecessary.

A **preliminary curettage** (to eliminate the possibility of malignancy) followed by uterine application of 800 to 1200 mg hrs. of **radium** is the ideal treatment for *menopausal uterine bleeding*. This procedure has given almost invariably excellent results. Keene and Payne also found that 600 to 700 mg hrs will control bleeding in 87 per cent. of menopausal women and reduce the incidence of menopausal symptoms to 19 per cent.

Although radium is most efficacious in controlling functional bleeding of the menopause, it is not advantageous to employ it in women of childbearing age. While it stimulates the ovaries, it also produces more or less severe endarteritis in the endometrium, thus interfering with subsequent function.

Low-dosage irradiation (**x-rays**) of the **pituitary** alone, or of both the **pituitary and the ovaries**, is of special benefit in the obstinate case of functional bleeding which resists hormonal therapy.

The dosage is  $\frac{1}{10}$  of the skin erythema dose (50 to 85 R units) applied to the pituitary and ovaries simultaneously, once a week for a period of 3 weeks. This method of therapy was employed in 6 cases of uncontrollable menorrhagia and metrorrhagia. One young patient received irradiation of the pituitary alone. Three of these patients were pubescent girls, while the other 4 were mature women. The entire group was cured, with a return of menstruation, normal in rhythm and duration.

The effectiveness of **x-ray therapy** is exemplified by the following report of a patient suffering with menorrhagia of functional origin, in whom this treatment was employed before the practical availability of hormonal products. The patient, aged 32, had had prolonged periods for 4 years prior to 1920. In March, 1930, she had a flow lasting a month, for which thyroid was given but without effect. On June 3, 1930, she was given x-ray therapy to the pituitary and ovaries in following manner:

<i>Amount of Irradiation</i>	<i>Region Treated</i>	<i>Date of Treatment.</i>
$\frac{1}{6}$ erythema dose .	Ovaries	May 8, 1930
$\frac{1}{6}$ erythema dose .	Right pituitary	May 12, 1930
$\frac{1}{10}$ erythema dose .	Ovaries	May 17, 1930
$\frac{1}{6}$ erythema dose	Left pituitary.	May 20, 1930
$\frac{1}{6}$ erythema dose	Ovaries	May 23, 1930
$\frac{1}{6}$ erythema dose . . . . .	Right pituitary	May 27, 1930

When the patient was again seen on September 26, 1930, she gave the history of regular and normal periods since the institution of x-ray treatment

**Summary.**—Functional or essential uterine hemorrhage may occur at any period during the active sexual life. It is, however, especially prone to affect women approaching the menopause. The condition may manifest itself as merely prolonged menstrual flows or as continuous or intermittent hemorrhages lasting a few weeks to several months or longer.

The endometrium assumes characteristic appearances in cases of functional uterine bleeding. The stroma and the glandular structures are enormously overgrown. The glands especially are markedly increased in number and are arranged in a disorderly fashion. Large cystic glands are often observed alongside narrow ones, producing the so-called Swiss-cheese pattern.

During the active bleeding phase the curetings of the endometrium show, in addition to the features described, areas of necrosis, thrombosis of vessels, and an extensive infiltration with polymorphonuclear leukocytes.

The uterine hemorrhage is the outward evidence of a more or less pronounced endocrinopathy. Abundant evidence is at hand indicating that ovarian dysfunction, either primary or secondary to pituitary or thyroid hypofunction, is the direct causative factor of the majority of cases of functional menorrhagia. In the woman of childbearing age, the bleeding is the direct outcome of an imbalance between the 2 ovarian hormones, estrin and the luteal hormone, progesterin. The ovarian imbalance may be induced by deficient function of the anterior pituitary lobe, either primarily or secondarily, as a sequel to thyroid deficiency.

Insufficient stimulation to the ovaries from the anterior pituitary lobe, especially in the woman of childbearing age, prevents the normal cyclical change in the follicle, with the result that multiple cysts are ultimately produced (follicle cystosis). In premenstrual bleeding of functional type there is a natural decline in the ability of the ovary, because of structural changes, to respond to normal pituitary and thyroid stimulation.

The failure of follicular ovulation results in faulty luteinization or an entire absence of corpus luteum formation. The continuous production of estrin from persistent ripe follicles is, therefore, unantagonized by progesterin, allowing the former to exert its influence unrestrained on the endometrium which becomes hyperplastic instead of progestational in character. External hemorrhage takes place as a result of degenerative changes in the hyperplastic endometrium by the process of rhexis or diapedesis.

Functional studies made on 10 young women suffering from functional menorrhagia have shown that there is *not* an excessive amount of anterior pituitary sex hormone in the blood. An absence of a demonstrable quantity of blood estrin was found in mature women with functional menorrhagia. It seems likely that the level of blood estrin varies with the stage (bleeding or non-bleeding) at which the test is performed.

From the physiologic standpoint, **progesterin therapy** should be the ideal method because of its neutralizing effect on estrin, and its ability to transform the hyperplastic endometrium into a secretory progestational type. In the absence

of a potent corpus luteum preparation, the administration of the luteinizing hormone of the anterior pituitary obtained from the urine of pregnancy (**prolan**) offers the next best therapeutic procedure.

The use of large doses of luteinizing hormone of the anterior pituitary (100 to 200 rat units daily, intramuscularly) is recommended as the most satisfactory method of treatment for functional bleeding in the young woman. Curettage is unnecessary except in cases of long-standing where the endometrial overgrowth is so excessive as to form polypoid masses. Hormonal therapy in such cases, after the curettage, prevents recurrences of the bleeding.

Twenty-one cases of functional uterine hemorrhage in women under 40 years of age were treated with preparations of anterior pituitary sex hormone derived from the urine of pregnancy. Good results were obtained by this therapy in all cases.

Experimental evidence is advanced suggesting that prolan (prepared from urine of pregnancy) in combination with nonsexual pituitary growth hormone (prepared from pituitary gland itself) should be a more potent ovarian stimulant than prolan alone.

It is still too premature to remark concerning the results to be expected from this combined therapy.

**Thyroid extract** is a valuable therapeutic adjunct especially in the functional menorrhagia of adolescence. Of 7 patients with severe menorrhagia of this type treated with thyroid extract, 4 were cured and 3 definitely improved. **Parathyroid extract**, in combination with large doses of a calcium preparation, is also beneficial in this condition.

Low dosage irradiation (**x-rays**) of the **pituitary** alone, or of both the **pituitary and the ovaries**, is recommended in the obstinate case of functional bleeding. This procedure is employed as a final resort in the event of failure of hormonal treatment and curettage. The dose is  $\frac{1}{10}$  of the skin erythema dose applied to the pituitary and ovaries simultaneously, once a week for 3 treatments. Six patients receiving x-ray therapy of the pituitary and ovaries, and 1 receiving pituitary irradiation alone, were cured of intractable uterine bleeding.

Finally, **diagnostic curettage** and an intrauterine application of **radium** (800 to 1200 mg hrs) is the ideal treatment in patients of the menopausal age. It is not advantageous, however, to employ radium in the woman of childbearing age because it is liable to produce destructive changes in the vessels of the endometrium which would interfere with subsequent function of the uterus.





# Gastroenterology

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**FOOD ALLERGY.**—*Relation to Gastrointestinal Disorders.*—J. Friedenwald and S. Morrison (Am J. Digest. Dis. and Nutrition 1:100 (Apr.) 1934) point out the importance of considering food allergy, since many of the symptoms arising from this condition may closely simulate organic gastrointestinal lesions. The symptoms of food allergy may be produced in two ways, *i. e.* (1) As a result of irritation within the digestive tract by the presence of foreign protein; or (2) as the result of a general allergic reaction following its absorption. The symptoms may be severe or mild, and in the latter, diagnosis is often extremely difficult. Rowe's findings in 100 cases are quoted. He found a family history of allergy in 65 per cent. Detailed findings on 50 cases are shown in Table I:

TABLE I

	Per Cent		Per Cent
Canker sores	20	Diarrhea	12
Coated tongue	18	Constipation	32
Heavy breath	14	Proctitis	2
Distention	32	Pruritus ani	4
Belching	26	Pain and soreness in epigastrium	20
Sour stomach	18	Pain and soreness in upper right quadrant	14
Epigastric heaviness	28	Pain and soreness in mid abdomen	16
Pyrosis	14	Pain and soreness in lower abdomen	20
Nausea	40	Ulcer type of pain	10
Vomiting	30		
Intestinal cramps	24		
Mucous colitis	14		

The authors present the chief complaints of 20 cases of gastrointestinal food allergy in Table II

TABLE II

	Cases	Per Cent.
Buccal canker sores	3	15
Indigestion (tullness, distention, eructations, acidity)	14	70
Nausea and vomiting (including sick headaches and migraine)	6	30
Intestinal colic	7	35
Mucous colitis	5	25
Diarrhea	3	15
Constipation	11	55
Upper right quadrant discomfort or pain	3	15
Epigastric discomfort or pain	2	10
Lower right quadrant discomfort or pain	2	10
Lower left quadrant discomfort or pain	1	5
Nervous dyspepsia	1	5

**Diagnosis.**—This is suggested by the history of other allergic phenomena, such as hay fever or urticaria, in the patient or in his family. The symptoms are more apt to develop later in the day, and occasionally some definite food relationship has been noted by the patient. Any digestive symptoms which do not fit into usual disease syndromes should suggest allergy, according to these writers. Physical examination is of little diagnostic value except to eliminate evidence of organic disease, or show evidence of skin manifestations of allergy.

Gastric analysis shows variable acid levels. The stools are not characteristic. Gastrointestinal x-ray may reveal signs of motor disturbances. In the authors' series hypermotility was found in 6 cases (30 per cent), pylorospasm in 4 (20 per cent), and spasticity of the colon in 5 (25 per cent). Eosinophilia is usually present. Skin tests are of value in many instances but usually must be combined with elimination diets for complete relief.

**Treatment.**—In the acute stages treatment consists of a **saline purge**, **gastric lavage**, if necessary, **enemata**. **Adrenalin chloride**, 10 to 15 minims (0.6 to 0.9 cc) of a 1:1000 solution, may give immediate relief. As soon as the offending agent can be discovered, absolute avoidance is essential. Later, gradual desensitization may be tried. **Calcium salts** in large doses are frequently beneficial, and may be associated with **parathyroid therapy**.

See also Section on DIETETICS

**GALL-BLADDER.—PHYSIOLOGY.**—A. C. Ivy and G. S. Bergh (J. A. M. A. 1:1500 (Nov. 17) 1934) review the present state of information concerning gall-bladder physiology.

**Absorption or Concentration.**—The gall-bladder concentrates hepatic bile from 4 to 10 times by removing chiefly water and certain inorganic constituents. In this process the bile becomes slightly acidified. In a fasting human the gall-bladder may store the entire 12 or 24 hour hepatic output of bile. In acute inflammation concentration does not occur, but in patchy inflammation or in involvement of the outer layers, concentration may be observed. The ability to concentrate and evacuate may return after subsidence of an acute inflammation. Cholesterosis usually does not interfere with concentration or evacuation unless associated with acute inflammation.

**Secretion.**—Normally there is a mucoid secretion from the gall-bladder wall, and a thick viscous material from the ducts. In obstruction with a functionless gall-bladder the ducts may be filled with this so-called "white bile." This same material may be present in association with hepatitis, with or without obstruction, and is of bad prognostic significance.

**Motor Activity.**—Two types of motor activity exist, *i. e.*, (1) rhythmic tonus changes, and (2) tonic contractions of the entire organ. The duct stimulus to contraction so far discovered is cholecystokinin, a hormone produced by the duodenal mucosa, by action of acids and fats.

**Sphincter of Oddi.**—The sphincter of Oddi can resist up to 75 cm. of bile pressure. The maximum expulsive pressure of the normal gall-bladder in dogs is 30 cm. Hence, spasm of the sphincter can prevent gall-bladder evacuation. Symptoms of sphincter spasm have been described by many authors under the terms hypertonic dyskinesia, cholepathia spastica, spastic distention, spastic dysfunction, and physiologic block.

After cholecystectomy, the sphincter of Oddi becomes incompetent and later partially competent in most instances, causing duct dilatation.

Some authors have estimated that in 10 to 20 per cent of patients who complain of biliary tract distress the symptoms are due to motor dysfunction of the gall-bladder and sphincter.

**Therapeutic Considerations.**—Daily evacuation of the normal gall-bladder by adequate fat intake may aid in prevention of gall-bladder disease. Its use antepartum is suggested. During *acute symptoms*, physiologic rest may be obtained by **withdrawal of fats, meats and acid fruits**. **Magnesium sulphate or oxide** may aid by relaxation of the sphincter. **Atropine** and **belladonna** are indicated for the same reason. The use of **bile salts** is not advisable in acute cases on the basis of present knowledge, although they may be of value in *chronic conditions*.

**Cholecystectomy.**—Removal of a severely diseased and nonfunctioning gall-bladder results in little if any physiologic disturbance, since a functional cholecystectomy has already been accomplished by the disease process. The removal of a functioning gall-bladder, however, may produce a train of postoperative symptoms, due to disturbed physiology.

**Effect of Drugs on Emptying.**—In their experiments on the effect of various substances on the emptying of the gall-bladder, W. L. Voegtlin and A. C. Ivy (Am J Digest Dis and Nutrition 1: 174 (May) 1934) found that cholecystokinin, pituitrin, and pilocarpine were the only substances injected into barbitalized dogs which caused actual muscular contraction of the gall-bladder. Cholecystokinin and pilocarpine act within a minute, while 10 to 18 minutes elapse before the effect of pituitrin is seen. Calcium chloride increased tonus rhythm. Methyl guanadine, choline, hydrochloric acid, hypertonic solutions of sodium chloride, cystine, various fatty substances (chyle, non-saponifiable oils), papaverine, epinephrine, ephedrine, magnesium sulphate, and peptone had no effect when injected intravenously. Atropine caused relaxation but did not prevent the action of cholecystokinin, while it did prevent the action of pilocarpine.

**PATHOLOGIC PHYSIOLOGY.**—The chemistry of bile in various pathologic conditions has been studied by I. S. Ravdin, C. Riegel, C. G. Johnston and P. J. Morrison (J A M A 103 1504 (Nov. 17) 1934). In patients with *chronic cholecystitis without stones* there was usually evidence of an increased concentration of calcium or bile salts or both. Patients with *chronic cholecystitis with stones* were divided into 2 groups, depending upon evidence of function as determined by cholecystography. As dysfunction increased, the chemical changes became more definite, these being a greater concentration of calcium, but a decrease in bile salt concentration, and usually a decrease in the bile salt-cholesterol ratio. No relation was found between the type of stone and the chemistry of bile removed at operation.

**DIAGNOSIS.**—**Intensified Oral Cholecystography.**—W. H. Stewart and H. E. Illick (Am. J Digest Dis and Nutrition 1: 337 (July) 1934) have combined the suggestion of Sandstrom of using fractional doses of dye with that of Antonucci of administering additional glucose during the procedure of cholecystography. They recommend the following technic in cases of faint or questionable visualization:

1 Previous to the first dose of dye, several cups of sweetened tea are given during the afternoon. One hour after the evening meal the first dose of dye is given by mouth. More tea and sugar are given during the evening

2 In the morning, no breakfast is allowed and films are taken at 12 and 16 hours after the first dose of dye.

3 At noon, a meal consisting of fruit juices, jello, fruit salad and sweetened tea is given, followed in 1 hour by a second dose of dye. More sweetened tea is given during the afternoon.

4 After an evening meal similar to the noon meal, a third dose of dye is given, followed by more sweet tea.

5 Films are taken the following morning, 36 hours after the first dose of dye

These last films usually show a very dense shadow if the gall-bladder is functioning. The authors believe the technic will lessen the occurrence of questionable shadows and make repeated studies less necessary, since faulty visualization in this method more definitely indicates pathology, and many more stone cases can be visualized.

**DISEASES OF GALL-BLADDER.**—In an effort to evaluate medical and surgical methods of treating gall-bladder disease, T R Brown (Am J. Digest. Dis and Nutrition 1 221 (June) 1934) considers the answers to two questions

“1. Has the patient gall-bladder trouble, and if so, what is its nature and severity?”

2 With gall-bladder disease certain or probable, what is the proper treatment?”

**Diagnosis.**—Concerning diagnosis, Brown stresses the importance of considering the biliary tract as a whole rather than the gall-bladder alone. This interrelation of the component parts of the system is based on anatomical and physiological considerations which must be remembered in studying any patient with symptoms suggestive of biliary disease. The most valuable diagnostic aid, according to Brown, is a carefully taken *history*. In his experience about 85 per cent correct diagnoses may be made by painstaking histories and physical examinations. Next in value the author places *cholecystography*. His statistics show an error of about 20 per cent by the oral technic (about 20 per cent of the cases diagnosed by x-rays were found to be normal and about 20 per cent of those diagnosed normal were found to be pathological at operation). The necessity of repeated studies in suspected cases is emphasized. The author has found little assistance in diagnostic *biliary drainage* although some physicians place considerable confidence in it. With these methods Brown feels that a correct diagnosis should be made in about 90 per cent of cases.

**Treatment.**—In determining treatment, the nature of the pathology and symptoms must be considered. The severe lesions such as suppuration, gangrene, perforation, frequent attacks of gall-stone colic, are always **surgical**, according to Brown (*loc cit.*) As to the time of operation, he feels that usually it is wise to wait until the most acute symptoms have passed, although evidence of progression of the lesion should be watched for and treated surgically without delay. The occasional occurrence of extensive pathology with little symptomatic or constitutional reaction is emphasized.

*Chronic cholecystitis* offers a greater field for disagreement between internist and surgeon. “Should we accept the view of certain surgeons and say that every

diseased gall-bladder should be removed as early as possible because by so doing a potential focus of infection will have been eliminated, and associated hepatitis and biliary tract infection usually will quickly subside, it will minimize the possibility of secondary lesions—pancreatitis, diabetes, persistent functional dyspepsia—and the possibility of malignant degeneration will be reduced to a minimum? Or, should one say it is in just this group of cases in which operation should be postponed indefinitely, if possible, because the dangers of waiting are far outweighed by the possible or probable postoperative sequelæ? What are these possible sequelæ? Among them are postoperative adhesions, a common duct stone, possibly sometimes pushed down into the common duct during the manipulation of operation, either of these often absolutely producing the original syndrome or producing a new syndrome often as bad, such as periodic attacks of greater or lesser obstruction or periodic attacks of biliary infection or even persistent low grade biliary tract disease, causing symptoms sometimes more severe than the original picture. The fact remains that functional disturbances often remain after gall-bladder removal and these have become so well established that they, not the underlying pathology, dominate the picture, or again one must appreciate the fundamental conception that certain of chronic 'gall-bladder' cases in reality present symptoms far more referable to diseased liver and biliary tract than to the gall-bladder alone, the gall-bladder playing but a minor rôle."

The author believes that prolonged drainage by means of **cholecystostomy** or **cholecystogastrostomy** is preferable to cholecystectomy in many of these cases.

In view of the acknowledged lack of any *medical* means of causing stones or adhesions to disappear, or a diseased wall to function, the author inquires what can be done nonoperatively for these patients. There are 2 main principles suggested. Minimize chances of reinfection of the biliary tract, and promote free biliary drainage. Focal infection, gastrointestinal irritation from unwise dietary habits, and colonic disorders should all be guarded against. Drainage may be promoted by **frequent feedings of fatty substances**, if well borne, and if jaundice is lacking, according to Brown (*loc. cit.*). **Salines** are of assistance, and in some instances **biliary drainage by tube** may be used. **Sedatives** and **antispasmodics** may be indicated. The author believes a large proportion of patients may be helped by these medical measures, and he has followed many for years during which time no evidence of progression or complication of the disease has occurred.

The author's statistics show a surgical mortality of 4.7 per cent. of 84 cases. Complete cures were obtained in 59 per cent., leaving 41 per cent. with continued symptoms.

**Treatment and Prognosis of Stoneless Gall-Bladder.**—E. A. Graham and W. A. Mackey (J. A. M. A. 103. 1497 (Nov 17) 1934) review the question of treatment of the stoneless gall-bladder. It has been found by many writers that unsatisfactory results are frequently obtained by surgery in this group of patients. In considering the prognosis after operation, it is important first to determine as closely as possible how large a part the gall-bladder contributes to the symptoms. In cases with severe symptoms, such as repeated colic, marked relief is expected;

in mild conditions the relief will be proportionately less. Particularly is this true if another unrelated condition also exists which may be responsible for many of the symptoms. Another group of patients who will be unrelieved by gall-bladder surgery are those in whom the chief cause of symptoms is a lesion not connected with the biliary tract but giving symptoms suggestive of gall-bladder pathology, such as diseases of the spine (osteoarthritis), chronic constipation, diseases of the right kidney, and duodenal ulcer.

A series of 161 cases is presented with the postoperative results judged after a year:

	Well	Improved	Un-improved	Post-operative Death	Total
Minimal lesion . . . . .	11	22	21	3	57
Cholesterosis . . . . .	14	2	14	1	31
Chronic catarrhal cholecystitis . . . . .	18	16	13	4	51
Chronic fibrous cholecystitis . . . . .	2	3	0	0	5
Cholesterosis with stone . . . . .	6	11	0	0	17
	51	54	.		161
	or 31.7 Per Cent or 33.5 Per Cent.				

The authors conclude that operations on the stoneless gall-bladder are unsatisfactory in about 40 per cent of cases. They believe there is little justification for operation in patients having only the beginnings of cholecystic disease.

**Incidence in Primary Anemia.**—The incidence of gall-bladder and liver disease in pernicious anemia has been studied by F. H. Bethell and B. D. Harrington (Am. J. Digest. Dis. and Nutrition 1:256 (June) 1934). They comment on the high incidence of potentially pathogenic bacteria in the upper digestive tract in the presence of achlorhydria, and suggest that the disease may be affected by this condition. The biliary tract is especially liable to involvement, according to these authors.

Fifty-eight patients with pernicious anemia were studied. Ninety-one per cent complained of digestive disorders other than sore tongue and anorexia, and 53 per cent of these patients obtained relief following remission induced by antianemic therapy. Intravenous cholecystography showed gall-bladder dysfunction in 22.5 per cent. Some of the patients showing evidence of gall-bladder disease proved very refractory to antianemic therapy.

**INTESTINES, DISORDERS OF.—AMEBIASIS.**—C. F. Craig (Am. J. Digest. Dis. and Nutrition 1:4 (Mar.) 1934) deplors the interchangeable use of the term "amebiasis" and "amebic dysentery." He defines "amebiasis" as the invasion of the tissues of man by the pathogenic ameba, *Endamoeba histolytica*, the invasion occurring primarily through the mucous membrane of the large intestine, which may be followed by symptoms varying all the way from slight digestive disturbances to the most severe symptoms of amebic dysentery or amebic abscess of the liver or other organs. By the term "amebic dysentery" is meant a symptom complex, characterized by a bloody, mucoid diarrhea caused by



*Endamæba histolytica* and occurring as one of the clinical manifestations of amebiasis.

The discovery of the parasite causing amebic dysentery was first made by Losch in 1875, and since then several species of nonpathogenic amebæ have been described, *i. e.*, *Endamæba coli*, *Endolimax nana*, *Iodamæba bütschlii*, and *Dientamæba fragilis*. Although originally believed to be largely a tropical disease, amebic dysentery has been reported from practically every state in the union, and it is estimated that from 5 to 10 per cent. of the population harbor this parasite, the incidence being greater in the southern states.

The life history of the parasite consists of 3 states. The active motile trophozoite occurs in the intestinal lesions and in the lumen of the bowel and may be passed in liquid stools. Under certain conditions the motile forms become round and motionless, the so-called pre-cystic stage, which later become cysts containing from 1 to 4 nuclei. These cysts are passed in the feces and may contaminate food or drink and reach a new host, where 8 small amebæ are developed which may invade the walls or encyst.

Normal gastric juice usually kills the motile forms, but the cysts are very resistant, and may live for days or weeks in water. Infection occurs from fecal contamination of food or water. Flies may harbor the cysts for as long as 48 hours in the intestinal tract and spread the disease in their droppings. The infected food handler is of the greatest importance as a source of amebiasis, however.

The *pathologic lesions* result from the combined cytolytic action of the parasite, its ability to penetrate and the secondary invasion of intestinal bacteria. The author stresses the fact that amebic ulcers may be present in asymptomatic carriers, and that hepatic abscess may occur in persons without dysentery.

**Symptoms.**—These are extremely varied, and often there is little to suggest the presence of amebæ. While actual dysentery is comparatively rare, considering the prevalence of the parasite, the author feels that recent outbreaks of severe symptoms warrant discussion of the acute symptoms.

The incubation period is extremely variable and the parasite may live for months or years in the intestinal wall without giving symptoms. The symptoms are also extremely variable, being rapidly fatal in some, while spontaneous remissions occur in others. Marked diarrhea with cramps and tenesmus and fever, or a gradual onset with recurring mild diarrhea, may occur. Physical signs in the acute stage consist of tenderness in the abdomen, especially over the cecum, ascending and descending colon. Liver pain and tenderness may occur and indicate hepatitis or early abscess. In chronic states the colon may be felt as a firm, indurated tube. Leukocytosis usually occurs in the acute forms, eosinophilia is not common, and an increasing anemia is the rule.

**Diagnosis.**—This depends upon the demonstration of motile forms or cysts in the feces. Craig (*Ibid.*) suggests stool cultures and agglutination tests for dysentery bacilli in all cases in which amebæ are found, since the two may co-exist. Direct microscopical examination of feces in acute cases will usually demonstrate the motile amebæ. Staining may be of assistance. In chronic cases concentration and search for cysts, and cultural methods are recommended. The

author's complement fixation test is of value but may be positive in some cases of chronic colitis of nonamebic origin, and the author feels that careful fecal examination is satisfactory.

**Prophylaxis.**—Craig (*Ibid.*) stresses the importance of careful **guarding of water supply**, and states that chlorination is of no practical value, since a very high concentration would be necessary to kill the cysts. **Boiling** is the only satisfactory method of rendering contaminated water safe. Food handlers should be periodically examined and if infected removed from work until treated.

**Treatment.**—In the acute stage of dysentery, treatment is best begun by **emetine**, according to Craig (*Ibid.*), but its use in carriers is not recommended. Not more than 12 daily injections of 1 grain (0.06 Gm.) should be used to control the dysentery. After the acute stage **carbarsone**, **treparsol**, **vioform**, and **chiniofon** are all recommended as efficient amebicides. The prognosis as to cure is not good in very long-standing chronic cases, regardless of the type of therapy used, according to Craig.

P. W. Brown (*Ibid.* 1:11 (Mar.) 1934) recommends a course of treatment as follows: (1) **Emetine hydrochloride**,  $\frac{2}{3}$  to 1 grain (0.04 to 0.06 Gm.), subcutaneously, twice daily for 3 days, and repeated after a week's interval. (2) **Treparsol**, 1 tablet (0.25 Gm.—4 grains), orally, with each of the 3 meals daily for 4 days, and repeated in 2 or more courses, allowing 10 days between each course.

Joseph Felsen (*Ibid.* 1:297 (July) 1934) suggests the following therapy:

**Emetine hydrochloride**, 0.03 Gm. ( $\frac{1}{2}$  grain) by mouth every evening and 0.065 Gm. (1 grain) subcutaneously every morning for 12 days. The drug should be stopped on any sign of muscular or heart weakness or nervous prostration.

**Chiniofon**, 0.5 Gm. (7½ grains) by mouth 3 times daily for 10 days. Daily enemata of 200 c.c. of 2 per cent chinoform in warm water to be retained are recommended by some.

**Acetarson**, 0.25 Gm. (4 grains) by mouth 3 times daily for 1 week, is recommended by some for the carrier stage.

**Vioform**, 0.25 Gm. (4 grains) in gelatin capsule, by mouth 3 times daily, for 10 days, repeated after a week if necessary.

**Carbarsone**, 0.25 Gm. (4 grains) in gelatin capsule, twice daily for 10 days, is recommended for chronic amebiasis.

Sidney Simon (*Ibid.* 1:486 (Sept.) 1934) suggests the use of **chiniofon** in larger doses than Felsen, using 3 tablets 3 times daily. He also recommends **carbarsone** but calls attention to the possibility of arsenical poisoning which may occur with this drug, but less frequently than with stovarsol or treparsol. This writer reserves **emetine** for only the acute phases of the disease. In some resistant cases the author recommends large doses of **powdered ipecac** (50 to 100 grains—3.24 to 6.5 Gm.).

**INTESTINAL ULCERATION.**—The pathology and differential diagnosis of various ulcerative intestinal diseases are discussed by J. Felsen (*Am. J. Digest. Dis. and Nutrition* 1:297 (July) 1934). In general, ulcerations may result from direct infection of the wall, as in typhoid or tuberculosis, from the

effect of toxins, either bacterial (dysentery, etc.) or chemical (mercury, etc.); from the direct action of protozoa, such as *Endamæba histolytica*; from vascular disturbances (emboli, or trophic ulcers); from neoplastic disease; and possibly from nutritional or metabolic disorders.

The *symptoms* of bowel ulceration are variable. Bleeding may be profuse in some acute conditions (typhoid, dysentery) or microscopic in some of the more chronic lesions (tuberculosis, malignancy). The earliest sign of intestinal irritation is excessive mucus production; later, the secretion becomes purulent. Cramps and tenesmus are usual complaints, and diarrhea is the rule, although periods of constipation may occur. If severe diarrhea occurs, dehydration and toxemia may be marked.

***Amebic Dysentery.***—Ulcerative lesions are usually found in the proximal colon, and slightly less frequently in the sigmoid. The ileum and appendix may be involved. The early lesions are discrete, rounded elevations with necrotic centers. The surrounding mucosa appears quite normal. Later, the typical ragged ulcers with undermined margins appear. The organisms burrow deep into the bowel wall and may invade the portal branches, thereby gaining access to the liver, where necrotic abscesses may appear.

The *symptoms* are extremely variable (see Craig, *Ibid* 1 92 (Apr) 1934) and the diagnosis depends upon demonstration of active amebæ or cysts in the feces, or the finding of typical ulcers and amebæ *via* the sigmoidoscope. The simultaneous occurrence of amebic and bacillary dysentery is not uncommon, according to this author.

(For *treatment*, see discussion of Amebiasis.)

***Bacillary Dysentery.***—This condition is produced by a variety of strains of the dysentery group of organisms. Felsen (*loc. cit*) divides them into 2 groups:

1. Shiga-Kruse, nonacid-producing in mannite, highly toxic, high mortality
2. Flexner-Strong, acid-producing in mannite, nontoxic, low mortality (The Sonne organism is included in this group.)

The lesions are largely in the colon and lower ileum and are apparently dependent more upon the toxins excreted in the bowel than upon actual invasion. The early lesions show swelling of the mucosa, with streaks or points of bleeding and some necrotic areas. Irregular superficial ulcerations follow; occasionally large sheets of mucosa are sloughed off. Strictures may result from the healing process.

Bacillary dysentery is usually a much more acute disease than amebic dysentery and the patient is much more toxic. The diagnosis may be suspected by the clinical course and the sigmoidoscopic picture, but confirmation depends upon culture of the organism from the bowel, or positive serum agglutination tests which may be found after 10 days or 2 weeks.

This type of dysentery is essentially a self-limiting disease, according to Felsen. Polyvalent immune sera have been used with varying success. Other treatment is supportive, aimed to combat the toxemia and dehydration.

***"Idiopathic" Ulcerative Colitis.***—This affects primarily the large bowel. The etiology is still in dispute and various bacteria have been reported as causa-

tive agents. Felsen does not believe there is sufficient evidence to accept any specific infection as the primary etiologic factor. He points out the nervous background of the disease and calls attention to a hypertrophy of the Meissnerian and Auerbach plexuses which may support the "trophic neurosis" theory proposed by earlier writers.

The earliest lesion is a swelling of the lymphoid follicles giving a granular appearance to the mucosa. Later, these tiny abscesses rupture, producing pinpoint hemorrhagic ulcerations. The membrane is diffusely involved but the disease may be limited to a relatively small segment of bowel. Gradual destruction of mucosa occurs and polypoid changes are frequent. Remissions may occur without treatment and the therapy often is unsatisfactory. The author recommends **oxygenation**, since the organisms primarily involved are anaerobic.

**Intestinal Tuberculosis.**—In adults, this is usually secondary and involves the ileum, cecum or colon. The disease usually starts in lymphoid tissue, which is destroyed, leaving an irregular ulcer with a necrotic floor and thick nodular margin. Circular, ulcerative lesions of the bowel usually result, although in the ileocecal region hyperplastic lesions may occur. This type of disease is difficult to differentiate from malignancy, nonspecific granuloma and "idiopathic" ulcerative colitis.

The *diagnosis* is suspected in the presence of systemic tuberculosis and an obstructive lesion in the ileocecal region by x-ray. Felsen states that in 85 per cent of cases of bowel tuberculosis, healed or active pulmonary tuberculosis may be demonstrated.

*Treatment* consists of **general measures**, and **bowel resection** in case of obstruction.

**Typhoid Fever.**—The systemic manifestations in typhoid fever are usually sufficient to suggest the diagnosis. A positive blood culture early in the disease, and a positive Widal after the third week, and recovery of the bacilli from the feces are corroboratory measures. Ulceration of the distal portion of the ileum usually occurs in the third or fourth week of the disease. Occasionally cecal ulceration may occur. Strictureing lesions are not common since the ulcers are usually linear.

**Malignant Disease.**—In colonic malignant disease about one-half of the lesions will be found in the rectum. According to Felsen, 69 per cent of rectal lesions appear in the lower 4 inches. Hemorrhoids are frequently associated. All colonic tumors tend to ulcerate, especially in the lower bowel. The diagnosis by endoscopy and palpation is usually not difficult although biopsy may occasionally be necessary. Beyond the reach of the sigmoidoscope, diagnosis must depend upon x-ray visualization of a defect in bowel outline. The author suggests barium enema with films also taken after evacuation, to aid in visualization of small sessile tumors or small ulcerations.

The *differential diagnosis* between circular scirrhous carcinoma and tuberculosis, and ulcerating carcinoma and amebic or tuberculous ulcerations may be extremely difficult.

Rarer forms of intestinal ulceration include syphilis, granuloma inguinale, and ciliate infestation (*Balantidium coli*).

**In Uremia.**—The various theories advanced to account for intestinal ulceration in uremia are discussed by R. H. Jaffe and D. R. Laing (Arch. Int. Med. 53:851 (June) 1934), who then present their findings in 136 cases of uremia coming to autopsy. It has been suggested that urea is secreted by the intestinal mucosa and is then changed to ammonium carbonate which acts as a caustic. Bacterial toxins are thought by some to produce ulcerations in the devitalized bowel mucosa. Others have suggested vascular degeneration associated with hypertension. Of the authors' cases, 27 per cent showed slight to moderate edema of the submucosa of the colon; 73 per cent. showed evidence of hemorrhage into the stomach, ileum, cecum or colon. Microscopic examination showed varying degrees of venous congestion, with extensive infarction and necrosis in the more severe cases. The authors conclude that the ulcerative changes seen in uremia are secondary to vascular change and submucosal hemorrhages.

**OBSTRUCTION OF UPPER PORTION OF SMALL INTESTINE.**—A. B. Rivers and N. W. Thiessen (Am J. Digest Dis and Nutrition 1:92, (Apr) 1934) have studied the problem of obstructive lesions involving the duodenum below the ulcer-bearing area and including the first 5 or 6 cm. of the jejunum. Lesions in this location produce marked toxic symptoms which have been shown to be largely dependent upon alteration in blood chemistry, dehydration and circulatory and renal failure. Other workers have demonstrated a histamine-like substance which apparently increases the toxic effect of obstruction.

The authors analyzed a series of 35 cases and found that 74.3 per cent of the lesions were in the mid portion of the duodenum, 8.6 per cent at the duodeno-jejunal angle, and 17.1 per cent in the upper jejunum. Over 65 per cent. were due to neoplasms.

Of the cases of mid-duodenal obstruction, 80.7 per cent were due to malignancy of the pancreas, duodenum, or gall-bladder, the remaining cases being due to inflammatory lesions.

The 3 cases of duodeno-jejunal obstruction were due to diffuse inflammation of undetermined origin, malignancy, and twisted mesentery, respectively.

The lesions causing obstruction of the upper jejunum in 6 cases were adhesions, inflammation, ulcer, tuberculosis, congenital band, and syphilis respectively.

**Symptoms.**—The average duration of symptoms in malignant cases was 5 years, and 9 years in benign obstruction. Rivers and Thiessen (*loc cit*) emphasize the fact that a long history does not necessarily rule out neoplasm. Many of the patients did not complain of *pain*, but when present, it was located usually in the epigastrium or upper right quadrant. *Belching* and *vomiting* were present in almost all cases, the vomitus containing bile in all but 2 cases, in which involvement of the common duct had occurred. *Constipation* was the most common complaint. The amount of *gastric residue* was variable, but only 5 cases showed less than 200 c.c. The degree of gastric acidity was variable. *Alkalemia* was present in 11 of the 23 malignant cases, tetany being present in two. In obstruction due to benign lesions, 4 of 12 had alkalemia.

**Diagnosis.**—It is frequently impossible to diagnose the type of lesion causing obstruction. Evidence of obstruction, however, is usually apparent. Repeated vomiting of large amounts of retained food indicates obstruction. If bile is present, obstruction below the ampulla is indicated. Gradual progression of symptoms, especially with the development of jaundice, favors malignancy. Usually the alkalemia responds to normal saline and glucose intravenously, failure to do so favors the presence of a malignant lesion, in the experience of Rivers and Thiessen (*loc. cit.*). Prompt surgical intervention is indicated if marked improvement does not follow three or four days of intravenous therapy.

**Treatment.**—This is outlined by Rivers and Thiessen as follows:

1. **Liquid diet** (broths, fruit juices, milk, etc.)
2. **Gastric lavage** twice daily
3. 1000 c.c. 10 per cent **glucose** in 1 per cent. **saline** given slowly twice a day. Larger amounts may be necessary if dehydration is extreme.
4. Sedatives such as **barbiturates** or **bromides**.
5. **Belladonna** is useful in some cases.
6. **Surgery** when patient is in best possible condition.

**REGIONAL ENTERITIS.**—P. W. Brown, J. A. Batgen and H. M. Weber (*Am. J. Digest. Dis. and Nutrition* 1:426 (Sept.) 1934) question the opinion of B. B. Crohn, L. Ginzburg and G. D. Oppenheimer (*J. A. M. A.* 99:1323 (Oct. 15) 1932) that "terminal ileitis" is a disease entity. They have seen cases of chronic inflammatory ulcerative disease of the jejunum, ileocecal region, and regional areas of the colon which pathologically are indistinguishable from the lesion described by the above authors in the terminal ileum.

The present report comprises 18 patients, in whom the diagnosis was confirmed at operation in 17 instances. The lesion was located in the ileum alone in 9, in the jejunum alone in 3, the terminal ileum and cecum in 1, and in the terminal ileum, cecum, and ascending colon in 5 cases. The lesion was localized and the intestinal wall was likened to a stiff rubber tube.

The histories were usually of several years' duration, with symptoms running a constant and progressive course. Only 5 of the patients had symptoms for less than 5 years. Ten patients had had previous operation, in 7 appendectomies had been done, in 6 of these an abnormal condition of the ileum or colon had been noted and was thought to be tuberculosis, Hodgkin's disease or inflammation of unknown etiology. One patient had had a splenectomy for a persistent anemia. The 3 remaining patients had been subjected previously to resection of the ileocecal portion of the bowel.

**Symptoms.**—In 16 of 18 cases the primary complaint was *pain*. This was described as cramp-like, colicky, knife-like, gripping, etc. In 2 of the 3 jejunal cases the pain was localized around and just above the umbilicus, the third had no pain, but complained of nausea. Of the 9 patients with ileal involvement, 4 complained of pain in the lower right quadrant, 2 had pain below and to the left of the umbilicus, 1 had pain about the umbilicus from left to right, and 1 had pain radiating from the gall-bladder area to the lower right quadrant. In the 6 cases with ileocecal and colonic involvement the pain was in the upper abdominal in 3, lower right quadrant in 2, and lower abdomen in 1 case. *Diarrhea* was

present in 6 cases, in all of which the lesion was found to be ulcerative. *Vomiting* occurred in 9 patients, being especially marked in the jejunal cases, but was not due to obstruction. *Fever* was present in 10 patients, and was intermittent. *Loss of weight* occurred in 14 of 18 patients. Vomiting, rest, fasting, laxation or enemas gave relief in some cases.

Intestinal fistulas were present in 2 cases. One-half the patients had a moderate or severe anemia. Leukocytosis was present in only 6 cases. Physical findings were usually of little assistance. X-ray findings depend upon the type of pathologic changes. Thickening, lumen narrowing with stiffening and shortening, and mucosal destruction may be demonstrated. Such studies demand close study of multiple observations of the progress meal as well as retrograde studies *via* barium enema.

**Differential Diagnosis.**—Tuberculosis must be considered in most of these patients. In those reported, chest x-rays were negative in all. Intussusception, disease of Meckel's diverticulum, appendicitis, carcinoma, actinomycosis and Hodgkin's disease must be considered. The diagnosis usually necessitates exploration.

**Treatment.**—Resection of the diseased bowel is usually necessary although in the cases reported several did well following ileocolostomy or enter-enterostomy.

**ULCERATIVE COLITIS.—Etiology.**—In discussing the etiology of chronic ulcerative colitis, T. T. Mackie (Am. J. Digest. Dis. and Nutrition 1:466 (Sept.) 1934) believes that there is considerable evidence that infection constitutes only a cog in the underlying mechanism. *Bacteriologic studies* have produced much conflicting data. In the author's 83 cases in New York City evidence of infection with strains of *B. dysenteriae* was obtained in 42 per cent. Similar findings were reported in 9 of 103 control cases without ulcerative colitis. His studies indicate to the author that the disease is not due to a specific infection, but that a variety of organisms, under specific conditions, may initiate or continue the pathologic process.

The possibility of *vitamin deficiency* playing a rôle in this disease was investigated in the present study comprising 75 patients. Sixty-three per cent of these patients showed some evidence of vitamin deficiency. These findings were more frequent in the more advanced stages of the disease. Table I indicates the frequency of the various findings.

Since a history of a deficient dietary was not obtained in most of these patients, the cause of the deficiency was obscure. It was felt that deficient absorption might be the determining factor. X-ray studies of the small intestine were done on 37 patients, and abnormalities were evident in 28 cases. The changes consisted of alteration of mucosal pattern, and derangement of motor activity. A normal small intestine was not found in any advanced case.

The possibility of *allergy* playing a part in ulcerative colitis is suggested by the sudden onset and subsidence of symptoms in some cases, and the effect

of vaccines and nonspecific protein therapy. Rowe suggests that food allergy may occur in about 30 per cent of people. The author studied 36 patients from this standpoint and found suggestive evidence of allergy in 77 per cent. Of these 28 patients, 18 gave a suggestion of food sensitivity with test diets, skin tests were of little assistance. It was found that in patients showing evidence of food allergy, all showed small bowel changes by x-ray, while there was no correlation between bowel changes and the bacterial allergic group.

TABLE I  
INDICATIONS OF "DEFICIENCY DISEASE" IN CHRONIC ULCERATIVE COLITIS

Clinical Classification	Stage I	Stage II	Stage III	Total Cases
Number of Cases . . .	28	38	9	75
Inflamed lingual papillae		23	8	31
Smooth atrophy of tongue		23	6	29
Oral aphthae		6	2	8
Skin lesions		4	7	11
Edema		3	4	7
Abnormal blood chemistry		2	4	6
Peripheral neuritis		1	0	1

The author concludes that chronic ulcerative colitis is probably the result of many factors. Table II summarizes his theory as to the possible mechanism

TABLE II  
MECHANISM OF CHRONIC ULCERATIVE COLITIS

STAGE I	Clinical phenomena limited to the gastrointestinal tract 1 Primary infection 2 Secondary infection 3 Allergic state—bacteria, food
STAGE II	Clinical phenomena not limited to the gastrointestinal tract 1 Secondary infection 2 Primary infection—present or absent 3 Deficiency states, incipient 4 Allergic state—bacteria, food
STAGE III	Deficiency disease dominant 1 Deficiency states, advanced 2 Secondary infection 3 Primary infection—present or absent 4 Allergic state—bacteria, food

**Treatment.**—J. A. Bergen (Am J Digest Dis and Nutrition 1: 190 (May) 1934) outlines the present day management of *uncomplicated* chronic ulcerative colitis. Rest, physical, mental and physiological, is especially necessary in this disease. Low residue diets aid in resting the colon. Local measures such as irrigations usually do more harm than good, according to Bergen. Complete rest of the colon by **ileostomy** is advised by some, but at the Mayo Clinic it is avoided since previous results were not favorable. **Immunization** by sera or vaccines prepared from the streptococcus frequently found by the author has apparently



produced good results if persisted in at intervals for months or years. A series of **blood transfusions** (250 to 300 c.c.) 5 or 6 days apart, for 3 or 4 injections, is recommended.

The **diet** should consist of foods which leave little residue for the colon to handle, such as beef, rice, white bread, Italian pastes, sugar, cooked and strained cereals, cooked eggs, butter and cream. Adequate calories should be given to maintain body weight. An ambulatory patient should receive about 3000 calories. Vitamins can be added in concentrated form.

TABLE III

## DIETARY REGIMEN FOR PATIENTS WITH CHRONIC ULCERATIVE COLITIS

"Foundation Diet" given on days 1 and 2\*

Breakfast	Dinner	Supper
Cereal, †bland, 1 serving, with	Meat soup without vegetables, 1 serving	Steamed rice, 1 serving
Cream, ½ cup and sugar	Meat, 1 serving (liver 3 times a week)	Meat or fish, 1 serving or 2 eggs
Bacon, 2 strips		Bread, white or rye, 1 slice or equivalent amount of biscuit, zwieback, cracker, etc
Egg, 1	Potato, 1 medium sized, any way except fried	Butter, 2 squares
Toast, 1 slice	Gravy, if desired	Bland dessert, ‡† no fruit, 1 serving
Butter, 2 squares	Bread, white or rye, 1 slice, or an equivalent amount of biscuit, zwieback, cracker, etc.	Cream, 2 tablespoonfuls
Coffee, if desired	Butter, 2 squares	Tea, if desired
Brewers' yeast‡	Bland dessert, ‡† no fruit, 1 serving	Sugar
	Cream, 2 tablespoonfuls	Brewers' yeast
	Tea, if desired	
	Sugar	
	Brewers' yeast	

The following foods may be added to the foundation diet as rapidly as the patient's condition permits

## "ADDITION DIET"

## Order of Additions

Days 3 and 4—One banana, very ripe, and codliver oil, 1 to 3 teaspoonfuls daily

Days 5 and 6—Orange juice, ¼ glass

Days 7 and 8—Vegetable puree, 2 tablespoonfuls

\*Given on admission, contains approximately 60 gm of protein and 2000 calories

†Cream of wheat, farina, puffed rice, puffed wheat, corn flakes, rice krispies and strained oatmeal

‡Brewers' yeast, 200 mg standardized vitamin fraction, is given with each meal

‡†Custards, cornstarch puddings, junkets, gelatin desserts without nuts or fruit, plain rice puddings, simple cakes and cookies, cooked fruit whips, and plain ice cream

ADDITIONAL DIET (*Continued*).

Days 9 and 10—Milk in the form of cream soup or milk toast.

Days 11 and 12—Whole milk, 2 glasses.

Days 13 and 14—Cream added to milk so that each of the 2 or 3 glasses taken contains half milk and half cream; bland fruit, canned or cooked peaches, apricots, pears, strained apple sauce, baked apple without skin, 1 serving

Days 15 and 16—Tomato juice,  $\frac{1}{2}$  glass or tomato jelly

Days 17 and 18—Whole cooked vegetable, 2 servings (puree, added on days 7 and 8, omitted) including, as desired, young tender carrots, beets, spinach, squash, peas, string beans, asparagus tips, potato any way except fried

Days 19 and 20—Shredded green lettuce, cut very fine Plain mayonnaise or cooked dressing may be used on the lettuce

*Drugs* have not proved of great value although **tincture of iodine** seems to have helped some patients, according to the author "Gentian violet by mouth in doses sufficient to color the stools blue definitely inhibits growth of streptococci. Arsenic in such preparations as treparsol, stovaisol, carbarsone or similar preparations, is dangerous." Mercury in the form of mercurochrome or metaphen is also not recommended **Iron** is indicated for anemia, the author recommending 3 to 4 Gm. ( $\frac{3}{4}$  to 1 dram) of reduced iron daily **Camphorated tincture of opium** and **codeine** are often indicated for relief of *cramps* and *tenesmus* **Bismuth**, **tribasic calcium phosphate** and **kaolin** may be helpful

All possible **foci of infection** should be **removed** at a time when the patient's condition can best stand the procedure Upper respiratory infections should be avoided, since the author reports that 57 per cent of relapses were initiated by such illness **Avoidance of mental and physical strain, care in eating and drinking**, and periodic courses of **diplostreptococcic vaccine** are recommended as measures helpful in preventing relapses

G. Schwartzman and A. Winkelstein (*Ibid* 1:582 (Oct.) 1934) have reported good results in treatment of chronic ulcerative colitis with **horse serum** of high titer against *B. coli toxy*. Conjunctival and intradermal sensitivity tests were first done. If negative, 0.5 cc., 2 cc. and 5 cc. were given intramuscularly at 6-hour intervals, during the first day. If no severe reactions occurred, intravenous injections were given during the next 48 hours in doses of 25 to 100 cc. until 300 cc. were given. Very slow injection was practiced. Urticaria was the rule in from 2 to 19 days. Good results were obtained in 18 of 21 cases so treated, in 15 of which the improvement was striking in from 2 to 6 days. No claim is made for the etiologic rôle of *B. coli* in this disease. The observed results are interpreted by the authors as possibly indicating the importance of *B. coli* as a secondary invader, or they may indicate the value of large amounts of nonspecific protein introduced within a short period of time.

**CANCER OF COLON.**—R. R. Graham (Am. J. Digest. Dis. and Nutrition 1:584 (Oct.) 1934) has analyzed 116 cases of carcinoma of the colon and 105 cases of acute intestinal obstruction. It was found that 18 per cent of all instances of acute obstruction were due to colonic malignancy. Seventy-five per

cent. of obstructing lesions in the colon were found to be malignant. The distribution carcinoma of the colon was found to be:

Rectum . . . . .	40	} cases	63 per cent. of total	
Sigmoid . . . . .	33			
Transverse colon . . . . .	12			"
Cecum . . . . .	12			"
Ascending colon . . . . .	11			"
Descending colon . . . . .	8	"		
<hr/>				
	116	"		

All of the acute obstructing colonic lesions were in the left colon. The type of lesion most frequently encountered was the annular constricting lesion, and secondly the large fungating type of carcinoma. This latter type is usually found in the rectum or cecum. Chronic bleeding with severe anemia is common in this type, and the author suggests that any patient having an unexplained severe anemia should be considered as having carcinoma of the colon until this diagnosis is disproven. Furthermore, any patient showing blood in the stool, in the absence of hemorrhoids or any bleeding lesion of the rectum and lower sigmoid, by sigmoidoscopy, and in whom gastric malignancy and peptic ulcer has been disproved, is probably suffering from carcinoma of the cecum, according to this author.

In *diagnosing* chronic obstruction due to malignancy Graham suggests suspecting every patient past 40 years of age who for the first time begins to suffer from increasing constipation. An exception is sometimes seen in cecal cancer, which may change the bowel habit from constipation to daily movements or diarrhea. Gradually increasing girth of the abdomen is a suggestive sign of chronic obstruction. Nausea and vomiting are rare in large bowel obstructive lesions. Frequently the early symptoms of obstruction are benefited by a program to combat constipation, so that a correct diagnosis is delayed. Rectal digital examination, a flat plate of the abdomen, barium enema, and, in questionable cases, sigmoidoscopy are indicated.

In the author's series the average duration of symptoms was 9½ months, varying from 3 weeks to 2 years.

In *treating* these lesions the author stresses the necessity of relieving the obstruction first, then later attacking the malignancy. The mortality of attempting partial or complete removal in the face of obstruction is very high, while that of **palliative colostomy** is only about 8 per cent., according to the author's statistics.

**FUNCTIONAL DISORDERS OF COLON.**—H. L. Bockus and J. H. Willard (Pennsylvania M. J. 37: 645 (May) 1934) call attention to the frequency of functional colonic disorders, having found these disorders to be a primary cause of symptoms in 46 per cent. of 1000 office records. A classification of these disorders is suggested:

- 1 Colonic neuroses (irritable or unstable colon)
  - (a) Motor neurosis—disturbance of tone and rhythm (spastic colon).
  - (b) Secretory neurosis—neurogenic mucous "colitis."
  - (c) Mixed neurosis—spasm and neurogenic mucus.

- 1 Colonic neuroses (*Continued*).
  - (d) Nervous diarrhea—nonorganic hypermotility
- 2 So-called anomalies or anatomical abnormalities of the colon
  - (a) Colonic redundancies (loops, reduplications).
  - (b) Coloptosis, including low cecum
- 3 True anomalies or embryonic abnormalities.
  - (a) Anomalies of rotation (1) Complete failure to rotate—left-sided colon (2) Incomplete rotation—high cecum.
  - (b) Anomalies of fixation. Lack of attachment of descending or ascending colon
4. Simple constipation

In the first group—*colonic neuroses*—the authors have analyzed 50 cases for statistical purposes. It was found that 86 per cent. were under 50 years of age. Jewish and Southern Europeans were more frequently affected. Most of the patients were classified as being of the intellectual type, or neurotic, or tense. Neurasthenia, the fatigue syndrome, insomnia, introspection, emotionalism are frequent nervous phenomena. The importance of the nervous background was emphasized by a definite relation of attacks to nervous upsets, and relief of symptoms by rest and relaxation. The symptoms consisted of constipation, diarrhea, alternating constipation and diarrhea, mucous discharge, abnormal stools, abdominal distress, relief by bowel movement, expulsion of flatus or enema, and duodenal ulcer syndrome.

The *diagnosis* necessitates elimination of organic colonic disease. Sigmoidoscopy and barium enema x-ray study are usually necessary. The chief x-ray signs of "irritable" colon are narrowing (62 per cent. of this series), zonal spasm (58 per cent.) and "prediverticulosis" (30 per cent.). Elongation, lack of, or shallow, haustral markings are frequent findings.

The authors feel that neurogenic mucous colitis is closely related to the "irritable" colon just discussed and differs only in the excessive secretion of mucus. The symptoms, findings and treatment of the two conditions are identical, according to these authors. For this reason they suggest the term "bowel neuroses," with subdivision into motor, secretory, and mixed types.

Nervous diarrhea is not included in the above group because evidences of unusual spasm or secretion are lacking, the chief feature being hypermotility.

In discussing the *anomalies*, the authors are hesitant to ascribe symptoms to this factor alone, although at times ptosis or redundancies undoubtedly contribute to the symptomatology. They agree with Kantor that "congenital anomalies may cause symptoms in all their owners some of the time, in some of their owners all the time, but are under no obligation to cause symptoms in all their owners all the time." They feel that usually symptoms are dependent upon superimposed spasm or inflammation rather than upon the anomaly *per se*.

Simple colon stasis or constipation is the most prevalent type of functional colonic disturbance, according to Bockus and Willard. The normal cycle of defecation is complex and depends upon a number of factors, a disturbance of any of which may result in constipation. Voluntary neglect and unwise use of laxatives and enemas are frequent primary causes, although there may be associated conditions such as spasm of the colon, redundancies, ptosis, atony of colonic or abdominal muscle, improper diet, etc.

An analysis of symptoms and findings in 100 cases of functional disorders of the colon is presented with a comparison between the neurogenic and the non-neurogenic groups:

Symptoms	Bowel Neuroses	Nonneurogenic Disorders
	60 Cases Per Cent.	40 Cases Per Cent.
Abdominal cramps . . . . .	35 0	12 5
Abdominal pain . . . . .	33 0	27.5
Duodenal ulcer syndrome . . . . .	16 6	2.5
Post-prandial dyspepsia . . . . .	40 0	35 0
Flatulence . . . . .	25 0	25.0
"Cardiac" syndrome . . . . .	10 0	17 5
Nausea . . . . .	8 3	22 2
Vomiting . . . . .	10 0	10 0
Nervousness . . . . .	26 6	22 2
Weakness and fatigue . . . . .	31 7	40 0
Headache . . . . .	21 7	40 0
Dizziness . . . . .	20 0	15 0
Constipation . . . . .	53 3	85 0
Diarrhea . . . . .	18 3	2 5
Alternating constipation and diarrhea . . . . .	13 3	7 5
Signs		
Ptoxis . . . . .	31 7	65 0
Redundancy . . . . .	30 0	27 5
Atony and dilatation . . . . .	1 7	30 0
Catarrhal proctitis . . . . .	3 3	35 0
Melanos coli . . . . .	0 0	10 0
Achylia gastrica . . . . .	8 3	2 5

The authors comment on the higher incidence of coloptosis and dilatation of the colon in the nonneurogenic disorders, and also the infrequent finding of evidence of catarrhal proctitis in the irritable colon group.

**Treatment.**—The most important feature in treating these cases is establishment of normal bowel function. Usually this involves the treatment of constipation. The authors' suggestions may be outlined as follows:

(A) *General*

1. Instruction of the patient in the normal hygiene of defecation
2. Institution of regular hours of eating, sleeping and defecation
3. Ample intake of fluid
4. Ingestion of ample dietary essentials—protein, fat, carbohydrate, cellulose, vitamins, minerals.
5. Abstinence from irritating laxatives.

(B) *Irritable colon and mucous colitis*

1. Ample rest and relaxation.
2. Psychotherapy
3. Roughage-free diet in beginning.
4. Avoidance of very hot or very cold foods or drinks
5. Increase in bulk if colon is large—agar, kaolin, etc
6. Mineral oil if stools are dry
7. Magnesium oxide if laxation is needed
8. Small enemas or oil injections at beginning or during emergency
9. Antispasmodics and sedatives as needed.
10. Hot applications or warm rectal instillations, for relief of acute symptoms

*(C) Dilatation, atony, redundancy*

1. Increase bulk of diet—agar, kaolin, etc. (cellulose is poorly tolerated if irritability is associated).
2. Exclude putrefactive proteins at beginning (meat, fish, eggs, poultry) in cases with right colon stasis, ileal stasis or indicanuria
3. Lactose—30 to 90 Gm. (1 to 3 ounces) or *B. acidophilus* or buttermilk as aid in combating putrefaction
4. Strychnine and vitamin B in atony, and calcium and parathormone may be tried.
5. Colon irrigations, or saline aperients occasionally indicated in toxic cases
6. Abdominal support and weight gain in ptotic patients.

**LEAD POISONING.** —L. Crosetti and Forconi (Polichinco 41 516 (Sept.) 1934) observed some 200 cases of acute and subacute lead poisoning arising from flour contaminated by lead. They found the most constant and conspicuous symptoms to be a characteristic skin discoloration, basophilic degeneration of the red blood cells; gastrointestinal symptoms, consisting of anorexia, dyspepsia, epigastric pressure, epigastric and mesogastric cramps, nausea and vomiting, a characteristic metallic taste, and a sensation of constriction of the throat, abdominal colic in about one-third of the cases; obstipation usually, but diarrhea occasionally.

Objectively, there was always hypertrophy of the mouth mucosa, especially the gums with the typical black line and occasionally ulceration. Hypertension was present during the crises in many patients. Gastric analysis showed a tendency toward lowering of acid figures in a majority of the cases studied, this was not related to the occurrence or severity of the anemia. X-ray studies of the stomach were essentially negative. The colon frequently showed atony of the proximal portion. Hepatic enlargement was frequent and some degree of jaundice was almost constant. This the authors believed to be a combination of hepatocellular damage and hemolysis. In one fatal case marked evidence of damage to the liver parenchyma was found.

There was frequent occurrence of albuminuria associated with pus cells in many cases and casts in a few. Water tolerance seemed normal, but ability to concentrate was frequently impaired.

A stubborn anemia was present in all cases, and anisocytosis, poikilocytosis, polychromasia, and granulocytosis were usually present. Basophilic stippling was present in practically every case. Cabot's rings and Jolly's bodies were infrequently found. Leukopenia, with relative or absolute lymphocytosis, was the rule. In 21 cases the sedimentation rate was determined and found accelerated in all but 4 of the patients. The rate was not proportional to the anemia.

Mental apathy and loss of memory were frequent nervous symptoms. Restriction and inversion of colored vision was found in 30 per cent of the patients examined.

**Treatment.**—This consisted of the use of **antispasmodics** to control the colic, attempts to increase **intestinal elimination**, and attempts to fix the lead with **calcium**. The authors recommend an intramuscular injection of **acetylcholine hydrochlorate** with an intravenous injection of **prostigmin** followed by **enemata**. The use of calcium by mouth and calcium intravenously did not

seem to be effectual in controlling colic. **Papaverine** and **atropine** seemed most effectual for this purpose. **Sodium iodide** apparently hastened recovery.

**LIVER.—JAUNDICE.—Differential Diagnosis.**—L. Schiff and F. A. Senior (J. A. M. A. 103:1924 (Dec. 22) 1934) have again emphasized the value of the *galactose test* in the differential diagnosis of jaundice. Patients with jaundice were studied for degree of icterus by means of the icteric index and van den Bergh determinations, and for evidence of obstruction by study of the stools, urine, and duodenal contents. In addition, the galactose excretion test and the bromsulphalein test were used.

In 50 cases of *acute catarrhal jaundice* a positive galactose test was obtained in 49, or 98 per cent. In two of these patients the primary test had been negative, but later tests showed a galactose excretion of more than 3 grams.

*Toxic hepatitis* from arsphenamine or cinchophen was studied in 15 patients, in 14 of whom a positive galactose test was obtained.

In 20 cases of *obstructive jaundice* from stone, carcinoma, pancreatitis, etc., negative galactose tests were found in all.

Eight cases of *portal cirrhosis* and 2 of *biliary cirrhosis* showed positive galactose tests in 4 instances; negative in 6.

A negative galactose test was obtained in 4 of 5 cases of hepatic malignancy.

In a series of 12 patients having had galactose tests, it was possible to study sections of the liver obtained at autopsy. Three patients giving positive galactose tests showed extensive diffuse liver damage. In two of these there were definite diffuse changes in the cytoplasm of most of the liver cells with some necrosis, and in the third, diffuse cirrhotic changes with pressure atrophy of areas of liver tissue. The remaining cases also showed varying degrees of liver change, but less evidence of widespread toxic liver-cell damage.

The authors conclude that this test is of great value in differentiating acute (toxic or infectious) jaundice from obstructive (extrahepatic) jaundice.

**ACUTE CATARRHAL JAUNDICE.**—L. J. Soffer and M. Paulson (Arch. Int. Med. 53:809 (June) 1934) studied, by means of the bilirubin excretion test, 11 patients from 2 months to 18 years after an attack of "catarrhal jaundice." Four of these patients were symptom free, and 5 had mild digestive symptoms. In 9 of 11 there was a definitely pathological degree of bilirubin retention. The suggestion is made that so-called catarrhal jaundice is not so innocuous as is usually believed.

**HEMOLYTIC JAUNDICE.—Treatment.**—E. C. Reifenshein and E. G. Allen (J. A. M. A. 103:1668 (Dec.) 1934) report their experience with **liver extract** in the therapy of chronic hemolytic icterus in three cases. The diagnosis of this disease depends upon the finding of an increased icteric index, urobilinuria, variable degree of anemia (possibly of the microcytic type), reticulocytosis, increased red-cell fragility, absence of bile in the urine, and presence of bile in the stools. Enlargement of the spleen, according to these authors, is not a necessary finding. The disease may be either congenital or acquired.

**Splenectomy** has usually been suggested as the most successful method of treatment, although it has been noted that increased blood fragility may persist, and occasionally hemolytic crises occur.

In the cases reported all were benefited by the use of liver extract. In one there was a persistence of slight icterus, urobilinuria and increased red-cell fragility, but in the other two the icterus, anemia and urobilinuria returned to normal. The fragility of red cells was not changed materially.

The authors do not recommend liver extract as a substitute for splenectomy, but believe it to be of value in some cases in which surgery is not warranted.

**JAUNDICE IN SYPHILIS.**—Increasing frequency of reports of the association of jaundice with syphilis led W. J. Wile and W. M. Sams (Am. J. M. Sc. 187:297 (Mar.) 1934) to review over 10,000 cases of syphilis for evidence of hepatic damage. A diagnosis of hepatic syphilis was made in 91 cases (0.9 per cent). Of this group 17 per cent had jaundice preceding any antiluetic therapy (0.18 per cent of the entire syphilis group studied). Following treatment with one of the arsphenamines, 1.35 per cent developed icterus which is about the average reported by other investigators.

Cases of postarsphenamine jaundice are separated into early and late cases. The causes of *early icterus* are thought to be: 1. Herxheimer reactions; 2. Toxic reactions, (a) due to overdosage, (b) due to susceptibility or idiosyncrasy. Herxheimer reactions occurred within 24 hours of the initial injection in patients with early syphilis. In 1 case jaundice followed excessive dosage in a chronic alcoholic. In the large majority of instances jaundice appeared after 2 or 3 treatments in patients who had shown some evidence of sensitivity to each injection. These signs were usually a febrile reaction, frequently preceded by a chill, and associated with a marked gastrointestinal reaction. A toxic exanthema appeared in about one-third of the patients who later developed jaundice.

In jaundice occurring *late* in treatment there is considerable uncertainty as to the etiology. Most of this group developed icterus several months after the initial series of one of the arsphenamines, the majority appearing between 80 and 100 days after the last injection. Theories advanced to explain this occurrence include:

1. Delayed toxic action of arsphenamine on the liver
2. Hepato-recurrence
3. Intercurrent infection ("catarrhal" jaundice)

Others factors may play a part, such as heavy metals, alcohol, malaria, pregnancy, etc.

It has been shown that arsenic may be retained in the liver for months, but arsenic has not been demonstrated in the livers of some of the fatal cases of late jaundice. Statistics lead the authors to believe, however, that arsenic does play a major rôle in the development of late jaundice. It is further believed that the evidence is not sufficient to show that hepato-recurrence is an important factor.

The differentiation between arsphenaminic jaundice and "infectious" jaundice ("epidemic" jaundice, "catarrhal" jaundice) is impossible in most cases. The authors compare the clinical findings in post-arsphenamine jaundice with those



of "infectious" jaundice in a series of cases and note the following differences in the two groups: (1) Asymptomatic onset and course are more common in the post-arsphenamine group. (2) Pain or tenderness in the abdomen is a bit more common in the infectious group, as are headache, malaise and weakness. (3) Constipation is more common and diarrhea uncommon in the infectious group. (4) Indigestion and loss of appetite are also more common in the infectious group. (5) The liver is more commonly tender in the infectious group, while the spleen is palpable a bit more commonly in the post-arsphenamine group. Blood counts did not give any differential aid. A possible relation between postarsphenamine jaundice and the incidence of infectious jaundice is suggested by the authors' statistics.

Pathologic studies indicate that the jaundice results from a severe intoxication and destruction of the liver substance analogous to other forms of poisoning possibly leading to acute yellow atrophy.

**Liver Function Tests.**—G. R. Biskind, N. N. Epstein and W. J. Kerr (Ann. Int. Med. 7 966 (Feb.) 1934) estimated liver function by means of the *rose-bengal dye* test in 152 patients with syphilis. These patients were selected because of a suspicion of hepatic involvement clinically, or because of jaundice at some period of treatment, or because of prolonged therapy.

Of the entire group 46 (30 per cent) showed evidence of liver dysfunction by this test. Seven had definite clinical evidence of hepatic diseases, and 13 had a history of jaundice. In the remaining 26 (56 per cent.) there was no evidence of liver disease except the abnormal retention of dye. No evidence of liver damage was found in many patients receiving large amounts of the arsphenamines over a long period of time. Most patients recovering from arsphenamine jaundice showed no residual damage, but in a small number permanent liver damage was observed.

**PEPTIC ULCER.**—Frank Smithies (Am. J. Digest Dis. and Nutrition 1 697 (Dec.) 1934) has analyzed a series of 500 cases of operatively-proved *gastric ulcer* (exclusive of malignancy and duodenal ulcer). In his experience the ratio of gastric to duodenal ulcer is 1:2.45. More than three-quarters of the patients were between 30 and 60 years of age. Males outnumbered females 2:1. No significant data were obtained regarding nationality, occupation, habits, dietetic errors, or previous infections. The incidence of other abdominal pathology is of interest. Thirty-six per cent had had appendectomies. In 1.4 per cent cholecystitis or cholelithiasis had been previously diagnosed or was noted at operation. There was a total of 50 per cent. showing evidence of disease of the appendix or gall-bladder at some period.

**Symptoms.**—The most striking symptom was the periodicity or intermittent character of the attacks. This type of history was obtained in 62 per cent. The flare-ups usually occurred in spring and fall, and the author suggests a possible relation to epidemic infections. Attention is also called to the close relation between the percentage of "cures" reported by several authors using various medical measures (70 per cent.) and the incidence of periodicity of symptoms (62 per cent.).

Fifty-two per cent. of the patients studied gave a history of 5 to 20 years' duration. Less than 20 per cent. gave a history of less than 5 years. Anemia and weight loss were common.

*Pain* was a symptom in 98 per cent and was described as discomfort, burning, gnawing, dull ache, soreness, colicky, tearing, piercing, etc. Opiates had been required in 94 per cent. The pain was referred to the right scapula, right costal margin, infra-navel region, between the scapulæ, at the sternum, throat, or to the nipples in two-thirds of the cases. In 83 per cent the pain bore a definite relation to food ingestion, occurring in less than 4 hours in most, 40 per cent had pain within 1 hour after food. In most cases there was definite relief by food ingestion, by dietary restriction and by vomiting. In this series *vomiting* had occurred in 74 per cent. Of the uncomplicated cases, 63 per cent vomited, while in those with some degree of obstruction, 85 per cent gave a history of emesis. *Pyrosis* was present in 82 per cent. *Hemorrhage*, either hematemesis or melena, occurred in 36.4 per cent. About 60 per cent of the ulcers which had bled severely were perforating to some degree. Ulcers which had once bled were prone to repeated bleeding.

The most constant *sign* was abdominal tenderness which was present in 93 per cent. The most frequent location was in the epigastrium in the midline or just to the right. *Gastric analysis* studies showed delay in emptying after a period of 12 hours in 67 per cent. In these patients with retention the average free acid was 56.4 and the total acidity 74.2. In nonretention cases the free acid averaged 40.5 and total acidity 52.4. The highest acid levels were met in acute and subacute perforating ulcers, while the more chronic ulcers gave figures compatible with carcinoma or gastritis. Blood, either microscopic or occult, was noted in 39 per cent. *Stool* examinations showed occult blood in 31 per cent (on meat free diets for 24 hours). The x-ray diagnosis of uncomplicated gastric ulcer (no stenosis, no scarring and no perforation) is largely accidental or inferential, according to Smithies. Fluoroscopy is usually of greater aid than film study, but both are advised. The author believes that the chief value of x-ray is one of corroboration, localization and characterization.

**Complications.**—**ALKALOSIS.**—The importance of an estimation of renal function before the administration of large doses of alkalis to ulcer patients is suggested by S. A. Wilkinson and S. M. Jordan (*Ibid.* 1:504 (Sept.) 1934). "Alkalosis" may produce headache, dryness of the mouth, mental depression, nausea, vomiting, stupor, and severe coma. The authors believe that decreased renal function is an important factor in patients showing alkali intolerance and a tendency to alkalosis. This conclusion is based on an estimation of renal function by the sulphate clearance test proposed by Macy in 1933. It was found that peptic ulcer patients with normal sulphate clearance tolerated alkalis well, while those with decreased clearance often manifested symptoms of alkali intolerance even to small doses. It was further found that evidence of renal damage by this test was present in a large proportion of ulcer patients. Renal deficiency was more frequent in patients with complications, such as hemorrhage and obstruction. These findings strengthen the previous impression that there is an association

to be discovered between alkalosis and hypertension, arteriosclerosis, and chronic vascular nephritis.

**HEMORRHAGE**—According to E. Kiefer (Surg. Clin. N. A. 14: 1073 (Oct.) 1934), the distinction between tarry stools and hematemesis is of little value in determining the location of the bleeding lesion. The ulcer most likely to bleed, according to this author, is located on the posterior wall of the first portion of the duodenum, a very vascular area close to the pancreatico-duodenal artery.

Gross hemorrhage occurs in about 20 per cent. of ulcer patients at some time in the course, according to this author. The *symptoms* consist of nausea and giddiness, fainting with or without hematemesis, shock if hemorrhage is severe. Severe bleeding is indicated by a falling blood-pressure, rising pulse, clammy skin, and pallor. Tarry stools appear at an irregular time later. Early blood counts are of little value in view of the compensating changes.

The *prognosis* depends upon the vessel eroded, the degree of sclerosis, and the degree of fibrosis of the ulcer. About 5 per cent. of the severe hemorrhages at the Lahey Clinic are fatal. Repeated hemorrhages in an arteriosclerotic patient of 50 years or older offer a poor prognosis. Hemorrhages have been found to bear a definite relationship to the incidence of recurrences of ulcer symptoms. Recurrence occurred in 30 per cent. in 2 years following 1 hemorrhage, and in 63 per cent. in 2 years following 2 hemorrhages. In the non-hemorrhage group of ulcer patients recurrence was found in 22 per cent. in 2 years.

T. Christiansen (Hospitalstid. 77 1023 (Sept 18) 1934) summarizes his experience in 289 cases of massive hemorrhage from gastric or duodenal ulcers. The total mortality under medical treatment was 7.9 per cent. There was a higher mortality in the group having the initial hemorrhage (8.97) than in those with recurrent hemorrhage (5.9 per cent.) Positive x-ray signs of ulcer were obtained in 60.8 per cent. Hypersecretion and hyperacidity were noted in 58.6 per cent. Patients with no previous ulcer symptoms seemed to have a slightly better prognosis than those with a long history.

*Treatment*, as suggested by Kiefer (*loc cit*), may be summarized as follows: (1) **Rest, elevation of foot of bed, external heat**; (2) **nothing by mouth** except for rinsing, (3) **morphine sulphate**,  $\frac{1}{6}$  to  $\frac{1}{4}$  grain (0.01 to 0.016 Gm.) every 4 hours, (4) pulse and blood-pressure every  $\frac{1}{2}$  hour during acute stage, (5) **transfusion** may be necessary if the hemorrhage is severe or the patient's condition very poor, but this procedure is best withheld if possible until bleeding has stopped, (6) **hypodermoclysis** may be given after 48 hours, (7) 1 ounce (30 c.c.) of water every hour may be started on the third or fourth day, and the **feedings** gradually increased by the addition of malted milk, gruel, and milk, (8) surgery is contraindicated during the acute stage unless hemorrhage is uncontrollable, (9) after two or more hemorrhages **surgical treatment** is advised.

**Diagnosis.**—*X-ray*—A. Ettinger and W. E. Davis (Am. J. Digest Dis. and Nutrition 1. 579 (Oct.) 1934) emphasize the value of the compression technic as advised by Akerlund and Berg, and the study of the duodenum in the oblique position, in determining the presence of and following the course

of *duodenal ulcers*. The exact localization of duodenal ulcers is of value in prognosis, since posterior lesions tend to gross hemorrhage and perforation into the pancreas, while anterior wall lesions are more apt to perforate into the general peritoneal cavity. By the compression technic the authors were able to visualize the niche in 50 per cent of 48 cases. The authors insist that a grossly deformed cap is not necessary in the diagnosis of duodenal ulcer.

In following cases with visualized niches through a course of treatment, the authors noted that while the symptoms often disappeared within a week, x-ray changes were not noted until after 6 weeks, and healing was often not apparent for 6 months.

**Prognosis.**—According to Smithies (*loc cit*), the prognosis of *gastric ulcer* is very difficult. Some ulcers will heal regardless of therapy, and others will occur, also regardless of therapy. "Each patient is a law unto himself." A careful history into the familial incidence of cancer is of importance since it is often impossible to differentiate a benign from a malignant ulcer in the early stage. The author believes that a certain percentage of benign ulcers later become malignant. This belief is based on an analysis of 566 cases of gastric cancer in which a long history suggestive of gastric ulcer was obtained in about two-thirds. Aside from cancer, complications such as stenosis, perforation, perigastritis, etc., developed in about 18 per cent, according to this author. In all, about 25 per cent of ulcer patients eventually die of the ulcer. Since 75 per cent do not die of the effects of their ulcer, the author believes these patients should be treated with optimism, since the fear often attendant upon the diagnosis often accentuates the patient's symptoms.

A statistical study of the end-results of medical and surgical treatment of ulcer has been reported by E. S. Emery (*Am J Digest Dis and Nutrition* 1:520 (Sept) 1934). The report is based on the effect of treatment on 1435 patients. Medical treatment gave relief to 13.7 per cent and surgical to 19 per cent, while 23.8 per cent of patients who received no treatment were relieved. However, of those receiving no treatment, 47.6 per cent were unimproved as compared with 12.7 per cent with medical treatment and 28.7 per cent with surgical treatment.

In uncomplicated patients 20 per cent of those receiving medical treatment were completely relieved as compared with 26 per cent treated surgically, however, 17.9 per cent of the surgical patients were unimproved as compared to 6.8 per cent of medical patients. Patients with retention of 30 per cent or more are best treated surgically, there is little difference in medical and surgical results in patients with less than 30 per cent retention.

**Treatment.**—The importance of close cooperation between surgeon and internist in the treatment of peptic ulcer is emphasized by Sara Jordan (*Surg Clin. N. A.* 14:1097 (Oct) 1934). "This cooperation should ideally be so integrated that if surgery is found necessary, previous medical treatment has given effective preparation, or at least has not been carried beyond the point where it becomes detrimental, rather than advantageous, to the patient." It is also necessary that medical treatment follow surgery in an effort to prevent

recurrence, and to improve function in the face of abnormal physiology secondary to surgery.

In presurgical care the patient should be instructed in the nature of his disease, and the probable prognosis of medical treatment. If surgery becomes necessary, then instruction should be given as to probable prognosis and the necessity for medical follow-up. Inadequacy of medical therapy must be judged both subjectively and objectively. Recurrence of distress does not necessarily mean recurrence of ulcer activity, since gall-bladder disease, pylorospasm, and colonic dysfunction may produce similar symptoms. In case the recurrent symptoms are quite definitely due to the ulcer, a decision must be made between further medical therapy or surgical intervention. In this decision the location of the ulcer must be considered, and the possibility of malignancy must be borne in mind. The resectability of the lesion is usually favorable in the lower portion of the stomach, but lesions of the cardia carry a high operative risk. Posterior gastric ulcers are frequently complicated by adhesion to the pancreas or small bowel and offer increased surgical risk, but are also refractory to medical treatment. In duodenal ulcers with high gastric acidity, palliative operations such as gastroenterostomy or pyloroplasty are often not successful in reducing gastric acidity, and recurrences of marginal or original ulcers are likely, according to this writer. Radical surgery (**partial gastrectomy**) is preferable if it can be accomplished, since it usually produces an achlorhydria which is seldom associated with recurrences.

After operation medical advice is of importance. The deranged physiology must be considered as well as the chemical and psychic factors of digestion. Later follow-up examinations will aid in preventing symptoms. The patient with continued hyperacidity and rapid motility must be more closely supervised as to diet and activity than the one with low acid and more normal gastric emptying. The author warns against concentrating too much attention on the gastric lesion to the exclusion of general advice to the ulcer-bearing individual. **Activity** and **rest** and **habits** must all be considered if the patient is to retain the benefit of any type of ulcer therapy.

*Aluminum Hydroxide*—Aluminum hydroxide has been suggested by I. H. Einsel, W. L. Adams, and V. C. Myers (Am. J. Digest. Dis. and Nutrition 1: 513 (Sept.) 1934) as an efficient drug to reduce gastric acidity. Previous studies have shown that aluminum is not absorbed in significant amounts. Administration to patients with ulcer has produced a lowering of increased gastric acidity in most instances to normal or subnormal levels after a period of several weeks. The preparation of the drug is of importance. It must be creamy white without unpleasant taste and must not induce nausea. It must be neutral to neutral red or phenolphthalein, and it must have a combining power when titrated with Toepfer's reagent of at least 100 c.c. of 0.1 N HCl per 4 c.c. of aluminum hydroxide. In this form the drug is not unpleasant to take and has the advantage of neutralizing acid without any absorption of alkalis.

The present report concerns the results of treatment of 110 cases of peptic ulcer. The usual regimen consisted of a **modified Sippy diet** of 6 daily feedings. Each feeding was followed in  $\frac{1}{2}$  to 1 hour by 1 to 3 drams (4 to 12 Gm.)

of gelatinous **aluminum hydroxide**. Very good results were obtained in spite of unsatisfactory living conditions of most of the patients treated. No untoward effects were observed except a tendency to constipation. No contraindications to the use of this treatment were found

*Bacterial Vaccines; Foreign Protein.*—D. J. Sandweiss and S. G. Meyers (*Ibid* 1 338 (July) 1934) have reviewed the literature on the use of foreign proteins and vaccines in the treatment of peptic ulcer and have added their results in 33 patients.

A polyvalent stock respiratory vaccine was used, being given subcutaneously twice weekly in ascending doses for 10 injections. After a period of observation a second or third course was used in some cases. Most of the patients had been tried on the usual diet-alkali program without satisfactory results. In the present series, 29 per cent. were not relieved of attacks by vaccine injections while remissions occurred in the remaining 71 per cent. The duration of remissions was less than 3 months in 35 per cent. and from 4 to 24 months in the remainder.

The authors conclude that vaccine injections may induce a remission but that cure should not be anticipated. This method should not replace, but should supplement, the usual therapy in selected cases.

*Insulin*—C. R. Jones (*Ibid* 1 135 (Apr) 1934) noted that in ulcer patients who were given insulin in an effort to induce weight gain there was a marked lessening of late post-meal distress, and a marked improvement in general health. Previous investigations had shown that in vagotonia, which is associated with peptic ulcer in 70 to 80 per cent. of cases, insulin lowered the vagus preponderance and lessened spasmodic tendencies.

In 12 patients with fresh, uncomplicated *gastric ulcer*, 10 to 20 units of insulin were given hypodermically 15 minutes before meals. The patients were allowed their usual diet, the only requirement being 100 Gm. (3½ ounces) of potato at each of two meals. After 4 or 5 days there was a distinct improvement in general health, a decrease in epigastric distress, and an increase in weight. There was usually an increase in gastric secretion, but a slight decrease in acid concentration. After 10 to 15 days, check x-ray studies showed no definite signs of ulcer. The duration of the improvement and evidence of decreased vagotonia was of uncertain duration.

Six patients with recurring ulcers were subjected to the same regime for 2 or 3 weeks with x-ray evidence of ulcer healing and symptomatic relief. These patients were followed for as long as 9 to 15 months without further recurrence.

In 8 patients with more severe ulcer pain and evidence of complications such as perigastritis, adhesions, etc., and no marked evidence of vagotonia, there was less definite improvement in digestive symptoms, but the general feeling of well-being was improved in all.

Recently the author has continued the use of insulin after the period of strict supervision in single daily doses for a few weeks, then every second day.

Patients in whom careful blood chemistry could be done showed a definite tendency toward a shift from acidosis to alkalosis on the insulin program. It has been shown by some experimenters that wound healing is delayed in an acid

medium, and that the beneficial effect of alkalis in peptic ulcer may be more humoral than in local neutralization of the gastric hyperacidity.

The author recommends first a **liquid diet**, then soft, then a solid diet, avoiding excessive roughage and condiments. Usually the diet may be stepped-up at weekly intervals so that a full diet is used after about 4 weeks.

*Okrin*.—A. J. Atkinson (*Ibid.* 1:713 (Dec.) 1934) reports the use of okrin (a powder obtained from mucilaginous material removed from okra pods) in 22 selected patients with peptic ulcer. Most of these were patients who had difficulty with other methods of treatment. There were 1 prepyloric ulcer, 8 recurrent ulcers after gastroenterostomy, and 13 duodenal ulcers.

Four to 8 Gm (1 to 2 drams) of okrin were taken in water, milk, canned milk, or milk and cream every hour while the patient was awake. Most patients also received 3 bland meals daily. Remissions occurred in 17 of the 22 patients in from 1 to 10 days. Most of the patients obtained marked relief of pain, pyrosis, vomiting, and night distress within 2 or 3 days.

The authors do not compare the results with okrin with those obtained with animal mucin, but state its advantages as being ease of administration, lack of unpleasantness, and lack of deterioration and putrefaction.

*Histidine*.—In the treatment of 52 cases of peptic ulcer with histidine by E. Bulmer (*Lancet* 2:1276 (Dec. 8) 1934), this remedy was used so far as possible as the sole treatment. Except in 3 cases, this has been ambulatory. The treatment consisted of daily intramuscular injections for 3 weeks of 5 c c of a 4 per cent solution of histidine, local and general reactions were not encountered and in 2 cases 20 c c was given daily for 3 weeks without demonstrable ill effects.

The immediate results of histidine treatment, if expressed in percentages, are 58 per cent of symptomatic cures with disappearance of the abnormal x-ray observations, 19 per cent. of symptomatic cures with persistence of some x-ray abnormality, and 23 per cent of failures. In a follow up, 3 patients relapsed and 1 of the apparent failures improved—the cases of gastric ulceration seem more amenable than those of duodenal ulcer, and those with a shorter history tend to react more favorably than those with a longer history. The results with histidine seem to be better than those of the more orthodox methods. Treatment on ambulatory lines has much to commend it.

L. Bogendorfer (*Munchen med Wchnschr* 81:1270 (Aug 17) 1934) used a preparation 1 c c of which contained 0.04 Gm ( $\frac{2}{5}$  grain) of histidine monohydrochloride in the treatment of 30 cases of gastric and duodenal ulcer. All other medicinal treatments were discontinued. The pains disappeared rapidly, and within a comparatively short time the patient could be put on an ordinary diet. Experiments are now being conducted to determine the influence exerted by the preparation on the gastrointestinal functions.

**STOMACH. — GASTRIC DIGESTION.**—In view of the claims of various food-faddists that mixtures of proteins and carbohydrates are not well tolerated by the stomach, M. E. Rehfuess conducted a series of experiments on patients hospitalized for a variety of disorders (*J A M A* 103:1600 (Nov. 24) 1934). No evidence of incompatibility between protein and carbohydrate was

found. The author concludes that while it may be true that many individuals overeat and are presumably better by a reduction in carbohydrates, "the unqualified acceptance of such teaching can lead to the occurrence of serious malnutrition as well as to a lighting of tuberculosis and old infections."

**GASTRIC SECRETION.—Bactericidal Action.**—Experimental evidence of the bactericidal activity of the stomach under a variety of conditions has been described by A. Hanszen (Am. J. Digest. Dis. and Nutrition 1:725 (Dec.) 1934). Water containing about 260 million *B. prodigiosus* and several hundred tiny paraffin-wax granules was administered to patients having varying degrees of gastric acidity, under varying conditions of alimentation. The beads were included to delimit the stools during further observations. Enemas were given 8 hours after the administration and plate bacterial counts were done.

In fasting individuals with undetermined gastric acidity plate counts indicated recovery of from 9 to 231 per cent of the ingested organisms. In this same group of persons the eating of a banana 1 hour before drinking the infected fluid produced an absence of *B. prodigiosus* in stool cultures in spite of the prompt appearance of the beads. Further study of the effect of "buffering" the gastric juice with banana pulp showed that this bactericidal effect was dependent upon 4 conditions, the omission of any one of which resulted in appearance of the bacteria in the bowel.

1. The first or uncontaminated meal must consist of a large quantity of well buffered material, in these experiments, banana.

2. The stomach contents must have an acidity greater than pH 2 just before contamination occurred.

3. The interval of time between the first and second meals must be between 20 minutes and 2 hours.

4. The interval between the second, or contaminated meal, and the next meal must be an hour or more.

It was further found that contaminated milk carried *B. prodigiosus* into the duodenum almost immediately if taken on an empty stomach. On the other hand, no bacteria were cultured from the duodenum of persons taking contaminated milk 1½ hours after eating 2 bananas. The author had previously shown that bananas produced an acid chyme in the stomach which remained highly acid for a "long period of time." If contaminated milk was put into a stomach containing enough buffered and acidified material so that after mixing with the milk the pH was still under 3, viable bacteria were absent in 5 minutes.

The author lists many foods whose buffering capacity has been tested. It is suggested that further knowledge in this field may be of considerable importance in preventing widespread gastrointestinal infections, especially in travellers in unsanitary countries and in armies.

**CANCER OF STOMACH.**—F. H. Lahey reviewed 168 cases of gastric malignancy (Surg. Clin. N. A. 14:1033 (Oct.) 1934). The age incidence was found to be:

Age 40 to 59 . . . . .	54 per cent
Age 60 to 70 . . . . .	35 per cent
Age 30 to 39 .... .	6 per cent.



Of the early lesions studied, 60 per cent. had had symptoms for 6 months or less. The operability of the lesion was found not to be dependent upon the length of history. Only 42 per cent of this series complained of epigastric distress. A mass was palpable in 31 per cent. of resectable lesions, and in 54 per cent. of inoperable lesions.

The author states that as a result of this study, it was concluded that there were no typical symptoms nor signs which could cause suspicion of cancer of the stomach. Weight loss, a distaste for food, vomiting in late cases, were some of the symptoms suggestive of malignancy. "One can only say that any unexplained digestive symptoms should be investigated by fluoroscopy and x-ray pictures of the stomach, together with gastric analyses."

At the Lahey Clinic 100 per cent. of lesions of the greater curvature have been found to be malignant. The next most frequent site is the prepyloric region; although in this area spasm, adhesions, and benign ulcer must be considered. Next in frequency is the posterior wall of the stomach, and least frequently are malignant lesions seen on the lesser curvature.

The author advises a medical program for a short period in suspected lesions, since even at operation the character of the pathology is often not apparent. If the lesion is benign, it should respond to a medical program by showing: (1) Symptomatic relief, (2) absence of occult bleeding in the stools, and (3) disappearance of the lesion by x-ray. All these criteria must be met or surgery is advised.

**Gastric Acidity.**—M. W. Comfort and F. R. Vanzant (Am. J. Surg. 26. 447 (Dec.) 1934) have reported gastric analysis findings in 805 cases of carcinoma of the stomach. A test meal of 8 arrowroot cookies and 400 c.c. of water were administered and an extraction taken in 1 hour. If acid was present, or if evidence of retention was found, the stomach was then completely emptied. In case no free acid or retention was present, extractions were continued at 15-minute intervals for another hour. The figures obtained were compared with the "normals" for age and sex previously established by Vanzant.

It was found that in carcinoma of the stomach the incidence of achlorhydria was about 3 times that "normally" found. The mean free acid was lowered about 14 units in males and 8 units in females. The range of free acidity in males was between 0 and 90, which is only about 10 units below the "normal" range. The gastric acidity was not markedly influenced by the degree of anemia, loss of weight, situation of the growth, or volume of gastric contents.

The patients were divided by history into groups: ulcer type, pseudoulcer type, and nonulcer type. In the *ulcer type* group the acid range was about normal, the mean free acid being only 5 to 10 units below the normal figures. In the *nonulcer type* group achlorhydria was about 4 times more frequent than in normal controls; the range of free acid was shortened by about 40 units, and the mean free acid was lowered by 20 units in males and 10 in females. In the *pseudoulcer type* group the figures lay between the other two groups.

The authors suggest that in the nonulcer type group carcinoma may develop in an anacid stomach, and in the ulcer group in a normally acid stomach. There

was nothing in the data to suggest that carcinoma developed on the base of an old ulcer

**FUNCTIONAL VOMITING.**—According to C H Drenckhahn and D. L. Wilbur (Am J. Digest. Dis and Nutrition 1:635 (Nov ) 1934), the clinical features of functional vomiting are characteristic. This condition usually afflicts young, unmarried women who present other psychoneurotic tendencies. The vomiting may be incited by fear, excitement, mental strain or shock, overwork, or mental depression. It often occurs periodically. The vomiting is usually easy, without nausea, trembling, cold perspiration or fainting. Most frequently the emesis occurs within an hour after eating, rarely after 2 hours; the patient is always able to reach a receptacle. Vomiting may occur frequently over a long period of time without any great effect on the general condition of the patient. A lowered basal metabolism is not uncommon.

Differentiation must be made from cardiospasm, pylorospasm, gastric and duodenal ulcer, carcinoma, etc. This is usually not difficult with a careful history, x-ray study, and laboratory findings. More difficult is the exclusion of diseases outside the digestive tract, such as pregnancy, Addison's disease, hyperthyroidism, organic nervous disease, gastric crisis, uremia, etc.

**Treatment.**—The treatment advised consists of the usual principles of caring for a neurotic patient, such as one physician, new environment, exclusion of over-zealous relatives and friends, hospitalization if possible. **Psychotherapy** is of great importance. Complete study with assurance of the absence of serious organic disease is often the key note of successful therapy. **Rest and sedation** are of great value. The authors suggest **withholding everything by mouth** for a few days, **substituting intravenous salt and glucose** and **proctoclysis**, later adding **small amounts of water** for a day or two and, finally, **increasing amounts of dry food**. Fluids should be restricted to small amounts and not given for 2 hours after other feedings. **Insulin** to stimulate appetite, **tube feeding**, **elevation of a lowered metabolic rate**, and occasional gastric lavage are measures which may be used if indicated.

# Hematology

*by*

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**BLOOD-FORMING ORGANS.**—The cells which circulate in the blood arise from 3 widely scattered centers of active cellular growth which have come to be called "organs." These are the bone-marrow, the lymphoid tissue, and the reticuloendothelial system.

(A) *Bone-marrow*—This, the most important of the blood-forming organs, is receiving increased attention as the result of recent studies. The sternal bone-marrow biopsy is receiving interested consideration. The sternum is easily entered by means of a hand trephine, a small plug of bone being obtained for sectioning and smears made on slides. Differential counts of the marrow in the sections have often proven of great diagnostic value. In the reviewer's hands, this procedure has proven of greatest value in the diagnosis of the often puzzling cases presenting chronic anemia, leukopenia, and thrombocytopenia, and has demonstrated that this triad of hematological signs is frequently due to aleukemic leukosis (*q. v.*).

(B) *Lymphoid Tissue.*

(C) *Reticuloendothelial System.*—Great numbers of articles continue to be written about this important group of phagocytic cells which is scattered throughout the body but is found principally in the liver, the spleen, the lymph-nodes, and the bone-marrow. The reviewer has cited the many activities of this "system" (New England J. Med. 210: 531 (Mar. 8) 1934) · the phagocytosis of foreign particles, the destruction of old red blood cells, the storage of fat, the formation of foreign body giant cells, the production of immune bodies, and the formation of the third type of white blood cells, the monocyte.

**BLOOD CELLS.—Terminology.**—For the red blood cells, terminology remains but little affected (*cf* New England J Med *loc cit*) The white blood cells have suffered some changes in terminology. Generally agreed upon are the following

*Bone-marrow Cells*—Myeloblast, myelocyte, metamyelocyte, mature polymorphonuclear cell. The metamyelocytes have been subdivided into "young" and "band" forms.

*Lymphoid Cells*—Lymphoblast, lymphocytes, large and small. The "plasma" cell is a form of lymphocyte.

*Reticuloendothelial Cells*—Histocyte, monocyte.

The word "monocyte" has come into general use and replaces the old term "transitional cell" as well as the ambiguous one of "large mononuclear cell."

**POLYMORPHONUCLEAR CELLS (GRANULOCYTES)**—Schilling, following the lead of Arneith, subdivided the polymorphonuclear cells into myelocytes, young forms, band forms, and segmented (mature) forms. The value of this subdivision in the study of infectious disease has been adequately demonstrated in hosts of papers. As an example of carrying the method out to its logical conclusion may be cited the paper of W. J. Crocker and E. H. Valentine (J Lab and Clin Med 20: 172 (Nov) 1934). These authors have added a large number of new indices, the value of some of them being questionable. The introduction of mathematics into such a variable tissue as the blood does not have strict scientific backing, and although it is possible to sit in a laboratory and prognosticate with a fair degree of accuracy what is going on in a given case of infectious

disease, it is sometimes of infinitesimally greater value to examine the patient. This should not detract, however, from any serious attempt to tabulate frequent exact findings in a given case of infectious disease and to interpret progress from them. The reviewer merely cautions against too literal an interpretation of hematological data in infectious disease, since these data should simply be regarded as another symptom or sign in a complex which, in its entirety, represents a diagnostic or prognostic interpretation.

**LYMPHOCYTES**—B. K. Wiseman (J A M. A 103.1524 (Nov 17) 1934) discusses the origin, physiology, and morphology of the lymphocyte. He states that the lymphocyte has a "definitive" life cycle similar in all respects to that of the polymorphonuclear cell and the erythrocyte. (This is not new, hematological treatises for many years have differentiated between primitive lymphocytes; large or immature lymphocytes often with dark blue cytoplasm, and small lymphocytes with pyknotic nuclei.) He points out that increased activity of lymphoid tissue is accompanied in the blood stream by increased numbers of lymphocytes, with increased concentration of basophilic substance in the cytoplasm (Cf the findings in "glandular fever," *q v*). It is axiomatic that hyperplasia of any of the 3 blood-forming organs is reflected to greater or less degree in the peripheral blood. Arnett and now Wiseman suggest studying the lymphocytes for variations in immaturity, the reviewer has found careful studies of this type of value in glandular fever and lymphatic leukemia.

**MONOCYTES**—The reviewer has discussed this cell in a number of papers and reviewed his findings in a recent article (New England J Med 210 531 (Mar. 8) 1934). Its importance has loomed large in recent literature, chiefly because of its association with the reticuloendothelial system, from which it is derived. The largest normal cell of the circulating blood, it is oval in shape and frequently irregular in outline. The cytoplasm is stained grayish blue with Wright's stain and contains innumerable very small violet granules. The nucleus occupies about 0.7 of the cell, is usually indented and bean-shaped in outline, and composed of a fine chromatin mesh. The reviewer has also directed attention to the appearance in the peripheral blood of what are probably either modified forms or actual precursors of the monocyte, *i e*, the histiocyte. This cell, extremely large, irregular in shape, with a spongy nucleus, frequently contains phagocytosed material and is found in conditions in which there is stimulation or hyperplasia of the reticuloendothelial system *i e*, in monocytic leukemia, chronic and subacute infectious diseases.

Wiseman (*loc cit*) also discusses the origin of the monocyte and its relationship to the "clasmatocyte" and demonstrates how knowledge regarding this cell has gradually been built up, particularly from the study of monocytic leukemia. The monocyte and the clasmatocyte are in all probability related cells, says Wiseman, since they appear together in experimental tuberculosis, and in the blood stream in monocytic leukemia. G. M. Levi and F. Penati in an extremely careful and complete piece of work (Arch. per le sc. med., 1934) discuss the fundamental experimental and clinical data bearing on the origin of the monocytes. They produced experimental reticuloendothelial reactions by the injection into animals of electronegative colloids and studied the resultant blood-picture. Ex-

perimental monocytosis was also produced with the bacterium *monocytogenes*, various vaccines, and experimental tuberculosis. These authors point out that a reticuloendothelial reaction in the tissues and monocytosis in the blood are not always correlated, and that it is possible to obtain a high grade of monocytosis without any hyperplasia of this system. They feel it is less difficult to derive the monocytes from the bone-marrow hemocytoblasts. In their second paper, Penati and Levi discuss clinical monocytosis and monocytopenia, infectious "mononucleosis," and monocytic leukemia in great detail, and the bearing of these conditions upon the various theories regarding the origin of the monocytes. They conclude that the monocytes are derived from hemocytoblasts (usually myeloid, at times lymphoid in origin), and that the doctrine which derives these cells from the reticuloendothelial system is not sufficiently documented. (Hemocytoblasts of the Ferrata type and histiocytes are in all probability synonymous terms. The sum-total of hemocytoblasts (histiocytes) found in the bone-marrow, spleen, liver, and lymph-nodes may be called the "reticuloendothelial system." There is in reality no strict divergence in views between the theory that the monocytes are derived from the cells of the reticuloendothelial system and that which states that they originate from hemocytoblasts.)

**RED BLOOD CELLS.**—The *reticulocytes*, immature red blood cells, have continued to be of first importance in the study of the anemias, particularly from the therapeutic standpoint. E. E. Osgood and M. M. Wilhelm (J. Lab. and Clin. Med. 19:1129 (July) 1934) state that the reticulocyte methods ordinarily in use give results which are too low. These investigators mix a small quantity of blood with brilliant cresyl blue in a test tube and then make smears. The normal percentage of reticulocytes by this method is frequently 2 to 4 per cent. W. Dameshek (W. Virginia M. J. 30:193 (May) 1934) showed that the reticulocyte response in hypochromic anemia following the use of inorganic iron varied directly with the extent of reduction in hemoglobin. At a hemoglobin level of 20 per cent, the maximal reticulocyte response with the use of an optimal dose of iron was 10 to 15 per cent. G. R. Minot (Tr. A. Am. Physicians 49:287, 1934) indicated the value of the "double reticulocyte response" in the study of the therapeutic potency of various extracts of liver. W. Dameshek and W. B. Castle (J. A. M. A. 103:802 (Sept. 15) 1934) used this method in assaying the potency of various commercial extracts of liver for parenteral use in pernicious anemia. First one extract was injected and daily reticulocyte counts obtained, after a 10-day period of observation, another extract was given in the same dosage. If a second reticulocyte response occurred, the second extract was definitely more potent than the first.

The *sedimentation rate of the red blood cells* continues to be widely utilized. T. H. Cherry (J. Lab. and Clin. Med. 20:257 (Dec.) 1934), after a careful analysis of the various factors which influence the sedimentation rate, comes to some very sensible conclusions, to which the reviewer subscribes. Cherry states that "to rely upon this test, without other laboratory data, is unwise. . . . From a clinical point of view, the sedimentation test alone is confusing, because individuals react biochemically to disease in different ways thereby producing variations in rate in the same pathologic state. As a prognostic aid it is of slight help.

The leukocyte count or filament—nonfilament study in conjunction with the clinical picture is of much greater aid than the sedimentation rate." So many articles are written which are enthusiastic about the outstanding value of the test in this field or that, that it is refreshing to read a critical article which places the test in its proper category: simply another symptom or sign (often misleading like other symptoms and signs) indicating an abnormal bodily state.

W. J. Stainsby (*M. Clin. North America* 18:911, 1934), in writing of the value of the sedimentation test, discusses its value in the neuroses. It is sometimes difficult to decide whether the patient's complaints are on a "functional" basis or composed of more solid stuff. With an elevated rate, considerable effort should be made to determine the underlying morbid process. Stainsby adds, however, that a normal rate does not rule out organic disease. He points out the value of the procedure in following the course of rheumatoid arthritis and in indicating the end of the active process in rheumatic fever and pulmonary tuberculosis.

**ANEMIA.—Etiology.**—Some of the most important advances in knowledge of anemia have been made in the understanding of the underlying etiological factors which are concerned. The bone-marrow, in which are formed all of the red blood cells, must be provided with a sufficient quantity of "liver substance" as W. B. Castle (*Ann. Int. Med.* 7:2, (July) 1933) has pointed out. This depends upon (1) a diet adequate in vitamin B<sub>2</sub>, protein, and iron, (2) a well-functioning gastric mucosa in which protein-splitting and iron-dissolving enzymes are present, and (3) a normally absorbing bowel.

*Diet.*—The importance of the diet, particularly its vitamin B content, previously stressed by Castle and Rhoads, was confirmed by Lucy Wills (*Lancet* 1:1172 (June 2) 1934) in her studies of the "tropical macrocytic anemia" and the "pernicious anemia of pregnancy" seen in India. The most striking work indicating the correlation of the diet, particularly that containing vitamin B<sub>2</sub>, with development of macrocytic anemia has been performed by C. P. Rhoads and D. K. Miller (*J. Exp. Med.* 58:585 (Nov.) 1933) on dogs. These investigators, by feeding the dogs a diet inadequate in vitamin B<sub>2</sub>, were able to produce glossitis, stomatitis, gastrointestinal disturbances such as diarrhea, severe macrocytic anemia, and a megaloblastic hyperplasia of the bone-marrow typical of that of human pernicious anemia. This disorder, if not too severe, responded to vitamin B<sub>2</sub> containing preparations but not to parenteral liver extract, indicating a different type of absorption mechanism in the dog as compared to the human.

L. S. P. Davidson and I. Leitch (*Nutrition Abstr. and Rev.* 3:901 (Apr.) 1934) take up in great detail the importance of a sufficient quantity of iron in the dietary, not only in humans, but in animals as well. They determined that "first-class animal protein" and green vegetables are deficient in the diets of the poorer classes and that these inadequacies may result in an iron-deficient anemia. The same mechanism holds true in the nutritional or milk anemia of infancy, as pointed out by H. W. Josephs (*Bull. Johns Hopkins Hosp.* 55:259 (Oct.) 1934). This author demonstrated by careful metabolic studies that the "birth-



stores" of iron derived from the mother were probably sufficient to last to the end of the sixth month under normal conditions. However, with a continued low iron diet, such as is found in an exclusive milk diet, and possibly on account of other factors, microcytic hypochromic anemia due to iron deficiency would develop.

*Stomach.*—Castle's epoch-making contributions which indicated so strikingly how intimately the condition of the gastric mucosa was related to the normal hematopoietic function have been abundantly confirmed. M. B. Strauss (J. A. M. A. 103:1 (July 7) 1934) reviewed the entire concept in an article on the rôle of the gastrointestinal tract in conditioning deficiency disease. Deficiency diseases, he brings out, are not only those in which a substance like vitamin C is lacking from the dietary, but may develop when the substance enters the body but fails to reach the essential organs concerned. *Pernicious anemia* is a "conditioned" deficiency disease because the deficiency is caused not by a defective diet, but usually by the absence from the gastric juice of a specific heat-labile factor (Castle's enzyme or "intrinsic substance"). It must be remembered that many cases of pernicious anemia have a strong dietary factor as well as a gastric factor and the disease probably does not develop in these instances until the diet becomes poor. Usually the cause for this lack of the specific enzyme from the stomach in a case of pernicious anemia is not clear, but some cases develop following gastrectomy, polyposis of the stomach, and diffuse gastric carcinoma.

R. Brown (New England J. Med. 210:473 (Mar. 1) 1934) investigated 151 autopsies of cases of undoubted pernicious anemia and found that 82 had gross lesions affecting the gastrointestinal tract. Forty-one of 42 histological studies of the stomach showed chronic gastritis with or without a loss of glandular epithelium; and in 37 the acidophilic cells had disappeared. She therefore concluded that achylia gastrica in pernicious anemia is due to a loss of acidophilic cells. P. J. Fouts, O. M. Helmer, and L. G. Zerfas (Am. J. M. Sc. 187:36 (Jan.) 1934) investigated the concept held by Morris and his associates that pernicious anemia was due to the absence of a "hormone" from the gastric juice. They concluded, (*Ibid.* 188:184 (Aug.) 1934) on the basis of experiments with gastric juice kept at different temperatures for varying lengths of time, and from other experiments in which the various gastric enzymes were separated by ultrafiltration, that the reason for the ability of Morris's gastric juice concentrate to induce a remission in cases of pernicious anemia was on account of the interaction which took place between Castle's enzyme and the globulin of the gastric juice (Castle had previously shown that normal gastric juice alone is not sufficient to stimulate hematopoiesis, but that an interaction between gastric juice and protein or vitamin B<sub>12</sub> was necessary). It has thus been adequately demonstrated that the normal gastric juice contains an enzyme, which is not rennin or pepsin, the function of which is to interact with protein or vitamin B<sub>12</sub> containing foods. The resultant substance after absorption by the bowel stimulates or nourishes the bone-marrow, so that normal red blood cell formation takes place.

It must not be supposed that the "intrinsic substance" of Castle is the only factor of importance in the gastric juice. Dameshek's previous work had suggested that the lack of hydrochloric acid in cases of chronic "primary" hypochromic anemia might be of causal importance. S. R. Mettler, F. Kellogg and J. F. Rinehart (Am. J. M. Sc. 186:694 (Nov.) 1933) in their study of 10 cases came to the same conclusion, *i. e.*, that the gastric dysfunction leads to failure in utilization of organic iron. This is also well brought out by the Italian investigators A. Allodi, F. Penati, and F. Quaglia (Minerva med. 1:489 (Apr. 14) 1934). It is likely that the hydrochloric acid of the gastric juice aids in the preliminary solution and digestion of organic iron. Its continued absence, possibly in the presence of other factors (dietary, hemorrhagic, etc.) leads gradually to an iron deficient state, *i. e.*, hypochromic anemia.

*Intestines*—That a normally functioning bowel is essential in the absorption of the hematopoietic stimulants formed in the stomach had already been postulated by W. B. Castle (*loc. cit.*). M. B. Strauss pointed out (*loc. cit.*) that macrocytic anemia indistinguishable from pernicious anemia may develop in the presence of various types of intestinal lesions such as celiac disease, idiopathic steatorrhea, and chronic stricture of the bowel. D. C. Hale (Brit. M. J. 2:162 (July 28) 1934) concluded that ulcerative colitis may bring about various types of anemia, whether macrocytic, microcytic, or a combination of both. That the gastric lesion in pernicious anemia may not be the only one present was commented upon by M. R. Brown (*loc. cit.*), who found that lesions of the intestines with enteritis were frequently present. It may thus be seen that anemia may develop (1) as the result of a diet deficient in (a) protein, (b) iron, (c) vitamin B, (2) as the result of some gastric defect, (3) as the result of some intestinal lesion. The latter two mechanisms are important in the development of the "conditioned" deficiency diseases among which pernicious anemia, primary hypochromic anemia, and pellagra are prominent.

*Other Factors*—Recent investigations have demonstrated that the liver is important in normal hematopoiesis. This had been suspected since Whipple and Minot's epoch-making investigations of the efficacy of liver in the treatment of anemia. M. M. Wintrobe and H. S. Shumacker, Jr. (Bull. Johns Hopkins Hosp. 52:387 (June) 1933), on the basis of 3 cases of macrocytic anemia associated with disease of the liver, suggested that the liver stores and possibly elaborates to some extent the hematopoietic "principle produced by the interaction of the intrinsic and extrinsic factors of Castle." Others authors, such as J. Van Duyn, Jr. (Arch. Int. Med. 52:839 (Dec.) 1933) and C. W. Heath (Folia haemat. 51:391, 1934), having taken up this attractive hypothesis. Heath states that the anemia in cases of hepatic cirrhosis is probably explainable on the basis of a loss on the part of the liver of the capacity of providing sufficient of the needed material for normal red cell formation. S. M. Goldhamer, R. Isaacs, and C. C. Sturgis (Am. J. M. Sc. 188:193 (Aug.) 1934) make an important contribution to this problem. By making extracts of human liver derived from a fetus, an inadequately treated case of pernicious anemia, an adequately treated case, a case of cirrhosis of the liver, and a case of acute yellow atrophy of the liver, and giving them parenterally to patients with pernicious anemia, these

investigators were able to demonstrate that the liver is probably a storage reservoir for "active principle." The anemia of cirrhosis of the liver may be due, these authors state, to failure of normal hematopoiesis to take place. These speculations, although attractive, probably do not give the entire explanation. It is likely that severe liver damage may be a factor in certain cases of anemia, but it is also probable that other factors must be present as well, such as an inadequate diet and an impaired gastrointestinal tract.

The importance of *pregnancy* as a factor in the development of anemia has been studied by M. B. Strauss (J. A. M. A. 102 281 (Jan. 27) 1934), who postulates that the fetus removes from the mother a definite store of "active principle" and of iron. In the presence of achlorhydria, the mother may be said to be vulnerable and unable to keep pace with this continued loss of substance to the fetus and anemia may develop. W. J. Dieckmann and C. R. Wegner (Arch Int Med 53.188 (Feb.) ; 345 (Mar ) 1934) have studied the blood of a group of normal pregnant women with great care and have demonstrated that anemia of a mild type develops in most of them, the anemia being most marked between the twenty-sixth and the thirty-fifth week.

The constitutional or *hereditary factor* probably plays some part, principally in pernicious anemia, possibly as well in primary hypochromic anemia. This has been mentioned by W. Dameshek (New England J. Med 210:531 (Mar. 8) 1934) and was recently emphasized by R. D. Friedlander (Am. J. M. Sc. 187:634 (May) 1934), who studied 500 cases of pernicious anemia. The latter author showed that the disease is largely confined to "those individuals endowed with a diathesis characterized by a fair complexion, light hair, blue eyes and achlorhydria." Pernicious anemia is a disease largely confined to the white race in temperate zones.

**Methods of Study.**—*Hemoglobin*—The reviewer (New England J Med 210 531 (Mar 8) 1934) has already noted the tendency in recent years to record hemoglobin in grams per 100 c.c. of blood rather than in per cent of normal. What is supposed to be normal has varied from method to method; it may be 13.8 by one method and 17.2 (gms per 100 c.c. by another. The Tallqvist and Dare methods have been found unacceptable by the reviewer and by W. J. Dieckmann and C. R. Wegner (Arch Int Med 53 188 (Feb ) 1934), the latter investigators also found the Sahli method unreliable, although if it is done with due care and if the tubes and standards are calibrated against the van Slyke oxygen capacity method, it will be found to be satisfactory. The Newcomer method, although seemingly more accurate, is frequently unreliable. Dieckmann and Wegner have found the Haldane-Palmer carboxyhemoglobin method most satisfactory. The reviewer is becoming more and more convinced that determination of the hemoglobin indirectly by determination of the blood iron should have far wider use. A. Sachs, J. E. Levine, and A. Appelsis (*loc. cit* 52 366 (Sept ) 1933) found that the average iron content of whole blood of 100 normal men was 50.01 mgs per 100 c.c., that of women definitely less. The iron content is roughly 0.3 per cent of the total hemoglobin.

*Mean Corpuscular Volume*—M. M. Wintrobe (Am J M Sci 185 58 (Jan ) 1933, Arch. Int. Med. 54 256, (Aug ) 1934), C. W. Heath (New

England J Med 209: 173 (July 27) 1933) and many others, have demonstrated that determination of the average volume of the red blood cell is an important diagnostic procedure, particularly in the diagnosis of the macrocytic anemias. The mean corpuscular volume is determined by first obtaining the volume of packed red blood cells per unit of blood. This may conveniently be done by centrifuging the blood in a Wintrobe 1 c.c. hematocrit tube (the blood is prevented from clotting by the use of dry sodium oxalate) and observing the volume of packed red blood cells. This figure per 1000 c.c. of blood (normally 460) is divided by the erythrocyte count in millions, the resultant figure being the mean or average corpuscular volume in cubic micra. Examples: (1) Hematocrit (volume of packed red cells per 100 c.c. of blood) 46, R B C 5.0 millions,  $M C V = \frac{46 \times 10}{5.0} = 92$  (2) Hematocrit 40, R B C 3.0 millions;  $M C V = \frac{40 \times 10}{3.0} = 133$ . Wintrobe gives the following figures: *normal or normocytic* 84-92, *macrocytic*, greater than 94, *microcytic*, less than 80 cubic micra.

*Red Blood Cell Diameter*—J. M. Vaughan and H. M. Goddard (Lancet 1: 513 (Mar. 10) 1934) compared the results obtained by mean corpuscular determinations with those obtained by determining the average cell diameters and concluded that volume can be regarded as a measure of cell size in pernicious anemia and in primary hypochromic anemia, but that there were occasional discrepancies, as in congenital hemolytic anemia, when the red cells are unusually thick and in certain other cases. The reviewer has found both methods to be of value, although the determination of the corpuscular volume is less time-consuming and laborious. The occasional discrepancies should be checked by careful examination of the stained blood smear.

**Classification**—The tendency in recent years has been to escape from the greatly involved, often meaningless, classifications of the past and to substitute for them a simple classification based on cell size or volume. M. M. Wintrobe (Arch. Int. Med. 54: 256 (Aug.) 1934) is one of the foremost exponents of this view, to which the reviewer heartily subscribes. Roughly, all cases of anemia may be classified as macrocytic, normocytic, and microcytic. The *macrocytic (large cell) anemias*, Wintrobe brings out, are characterized by an increase in the average red blood cell diameter to 8.0 to 8.5 micra and an increase in the mean corpuscular volume to above 94 cubic micra. The *normocytic anemias* have a normal red cell diameter (7.0 to 7.5 micra) and a normal average red cell volume (80 to 94). The *microcytic anemias*, which are usually hypochromic as well, are characterized by small average cell diameter (6.0 to 6.5 micra) and a low average red cell diameter (less than 80 cubic micra).

The most common of the macrocytic anemias is "pernicious anemia," but many other types are present, associated usually with deficiency in Castle's antianemic principle (see ETIOLOGY). Normocytic anemia is usually associated with decreased bone-marrow function (aplasia, hypoplasia). Microcytic anemia is associated with a deficiency in iron from the body and is seen particularly in chronic blood loss and in the chronic hypochromic anemia of middle-aged women with achlorhydria.

The above terms should be qualified by indicating the possible etiological factors present: thus,

Macrocytic anemia: Poor dietary, achlorhydria, diarrhea.

Normocytic anemia: Benzol.

Microcytic anemia: Achlorhydria, pregnancy.

**PERNICIOUS ANEMIA.**—Some of the most important advances in the past few years have been made from the standpoint of etiology (*q. v.*). The concept is gradually becoming established, as enunciated by W. B. Castle (*Ann. Int. Med* 7·2 (July) 1933), that pernicious anemia is not in reality a separate disease, but rather the end-result of many diverse factors, whether dietary, gastric, intestinal, or hepatic in origin. The end-result is a megaloblastic marrow with the resultant presence in the peripheral blood of macrocytes. It is important, therefore, in every case of suspected pernicious anemia to study very carefully the gastrointestinal tract and the diet.

**Diagnosis.**—It has struck many students of the disease that outspoken cases are on the decrease and that most instances are relatively mild as far as the anemia goes, although the neurological symptoms may dominate the picture. A. G. McGhie (*Canad. M. A. J.* 30·274 (Mar.) 1934) makes a plea for early diagnosis and stresses such symptoms as anorexia, sore tongue, paresthesias, and difficulty in locomotion, together with such signs as glossitis, diminished vibratory sensation, and increased reflexes. Neurasthenia, arthritis, some gastrointestinal disorders are all apt to be diagnosed, unless pains are taken to do very careful hematological work in these patients. W. Dameshek (*New England J. Med* 210 531 (Mar 8) 1934) has pointed out that early examples of "combined system disease" which is in reality part and parcel of the greater syndrome of pernicious anemia are often associated with what at first glance is an almost normal blood picture. However, careful investigation will usually show the following: slight reduction in red blood cells (3.5 to 4.0 million), high color and volume index, increased mean corpuscular volume, low white blood cell count, macrocytes with an increase in the average diameter of the red cells, presence of "pernicious anemia neutrophils," slight increase in icterus index and in bilirubin content of the blood, and complete achlorhydria. M. M. Wintrobe has pointed out (*Arch. Int. Med* 54.256 (Aug.) 1934) that the mean corpuscular volume is of utmost importance in diagnosis. The color index, depending as it does upon an accurate hemoglobin determination and an accurate erythrocyte count, is very frequently in error, but the corpuscular volume is easily obtained when the hematocrit determination and the red cell count are known. In making a diagnosis it is futile to wait until severe anemia is present and nucleated red blood cells are present in the smear. In the presence of (1) the findings indicating macrocytosis, (2) glossitis, (3) achlorhydria after histamine, and (4) neurological changes usually of posterior and lateral column involvement, the diagnosis of pernicious anemia is justified. The reviewer has pointed out in the above mentioned article that certain cases of aleukemic leukemia will simulate very closely all of the hematological features of pernicious anemia. With the presence of splenomegaly, and particularly when therapeutic response to liver extract does not take place, this possibility should be suspected. It is important above all else

in any case presenting neurological lesions, particularly those of the extremities, to rule out pernicious anemia, since treatment in the latter event may be so effective.

**Treatment.**—Advance in the therapy of pernicious anemia continues unabated. W. Dameshek and W. B. Castle (J A M A 103:802 (Sept 15) 1934) state that **liver** from the cow, the pig, the horse, even the codfish has been utilized and has been given in the form of a powder for oral use and in solution for parenteral administration. These authors state that parenterally given (intramuscular) solution of **liver extract** has been demonstrated to be 30 to 100 times as effective as orally administered extract. Thus, the material derived from 100 Gm. ( $3\frac{1}{3}$  ounces) of liver (if fully potent) when given intramuscularly is equivalent to 3000 to 10,000 Gm. ( $6\frac{2}{3}$  to 22 lbs.) of material given orally. There is, to be sure, some loss in potency in too great a "refinement" of extract, particularly when it is "concentrated" in small bulk. However, even with this loss of potency, a large amount of effective material is introduced when 3 c.c. ( $\frac{3}{4}$  dram) of solution containing the material derived from 100 Gm. ( $3\frac{1}{3}$  ounces) of liver extract is given intramuscularly. This is particularly valuable when the central nervous system is involved and has completely modified the prognosis for these cases.

Striking responses are often obtained with the persistent and extremely frequent use of the "concentrated" products of liver extract. When faced with a case of this type, it is the custom of the reviewer to inject daily doses of the material derived from 100 c.c. ( $3\frac{1}{3}$  ounces) of extract in the deltoid or gluteal muscles until definite improvement begins. This is followed by doses given every 2 days, then every 3 days, and when the patient is ambulatory, once weekly or even every 2 weeks. Some patients require weekly doses, others bi-weekly doses in order to continue hematologically well (50 million R.B.C.) and neurologically relatively free of symptoms.

Complete cure of the neurological symptoms is to be expected only in the mild cases showing paresthesias and slight to moderate loss in vibratory sense. In those patients presenting spasticity and ataxia, 50 to 75 per cent improvement in gait and in strength may be expected, although the reflex changes will persist almost unchanged. Those cases with posterior column involvement alone usually do better than those with lateral column involvement as well. Striking, even unbelievable improvement sometimes occurs and is indeed a contrast even to the results obtained with oral liver therapy. S. M. Goldhamer, F. H. Bethell, R. Isaacs, and C. C. Sturgis (J A M A 103:1663 (Dec 1) 1934) and R. R. Grinker and E. Kandel (Arch Int Med 54:851 (Dec) 1934) are, however, pessimistic regarding the effects of therapy.

The exact therapeutic effect of vitamin B containing products is still uncertain. L. S. P. Davidson (Brit M J. 2:481 (Sept 9) 1933) reviewed the therapeutic effects of **yeast** products in different types of anemia and concluded that some hematopoietic principle was present, although in small concentration. H. C. A. Lassen and H. K. Lassen (Am J. M. Sc. 188:461 (Oct) 1934) cite the conclusion of Strauss and Castle that the extrinsic factor "may now be defined as a substance closely related to vitamin B<sub>2</sub>, if not vitamin B<sub>2</sub> itself" (Castle,

in an editorial note in the same article, states that he is fully prepared, however, to relinquish this suggestion.) These authors concluded on the basis of careful experimental work that the "extrinsic factor searched for by Castle is not identical with vitamin B<sub>2</sub> nor with B<sub>1</sub>, and presumably not with any other fraction of the vitamin B complex." It is difficult to explain the often striking results obtained in cases of pernicious anemia with **marmite** (an autolyzed yeast product), unless other substances, as L. Wills and A. Naish state (*Lancet* 1:1286 (June 17) 1933), are present in this crude commercial product. D. K. Miller and C. P. Rhoads (*New England J. Med.* 211:921 (Nov. 15) 1934) state that "conclusive proof of the identity or lack of identity of the dietary anti-anemia factor and vitamin B<sub>2</sub> (G) clearly must be deferred until isolation of the vitamin in a pure form has been effected." This is a rather conservative conclusion, since these authors demonstrated that a rice-polishings concentrate after incubation with normal gastric juice gave a clear-cut reticulocyte and erythrocyte response in a case of pernicious anemia.

**PRIMARY HYPOCHROMIC ANEMIA** (Idiopathic Hypochromic Anemia; Achylic Chloranemia; Achlorhydric Anemia, Hypoferric Anemia; Chronic Hypoferrism).—*Pathogenesis*.—Various authors have confirmed the original findings of Kaznelson, Reimann and Weiner, Dameshek, Witts, Davies, and others regarding the presence of a so-called "primary" anemia with a "secondary" type of blood-picture (*i. e.*, low color index, achromia of the red cells, etc.) S. R. Mettier, F. Kellogg, and J. F. Rinehart (*Am J. M. Sc.* 186:694 (Nov.) 1933) found that the food intake was frequently deficient in iron and that the gastric contents were almost always completely achlorhydric. W. Dameshek (*J. A. M. A.* 100:540 (Feb. 25) 1933) pointed out that the disease was in all probability a chronic iron deficiency state and that the symptoms of early greying of the hair, wrinkling of the skin, sores about the mouth, atrophy of the tongue, brittleness and flattening of the finger nails were probably "trophic" disturbances dependent upon a lack of iron in the bodily cells. A careful study of the disease was made by the Italian investigators A. Allodi, F. Penati, and F. Quaglia (*Minerva med.* 1:489 (Apr. 14) 1934), who confirmed the above clinical findings and also expressed the view that the pathogenesis of the disorder was in great part linked up with a deficient function of the stomach. Recent studies have convinced the reviewer that most cases are associated with multiple etiological factors (as noted in chapter on ETIOLOGY). The diet is frequently deficient, the gastric juice is defective, and often an added factor of bleeding (menorrhagia, from hemorrhoids, etc.) is present. Multiple pregnancies are also important in the pathogenesis of the disorder.

*Treatment*.—The treatment of the condition, whatever the cause, is relatively simple. The body may be said to be in a state of iron starvation and large quantities of **iron** are necessary. Dameshek (*W. Virginia M. J.* 30:193 (May) 1934) determined the optimal dosage of iron for various preparations to be as follows. **ferric ammonium citrate** 3.0 to 6.0 Gm. ( $\frac{3}{4}$  to  $1\frac{1}{2}$  drams) daily (given either in the form of 0.5 Gm. ( $7\frac{1}{2}$  grain) capsules, in 25 per cent solution, or as the scale salt itself in 2 Gm. (30 grain) dosage dissolved in milk), **reduced iron** 3.0 Gm. ( $\frac{3}{4}$  dram) daily (given in 0.5 to 1.0 Gm. ( $7\frac{1}{2}$  to 15 grain) cap-

sules), **ferrous chloride-ferrous glutamate**, 4 Gm (1 dram) daily. In using these large doses of iron, it is wise to begin with a relatively small dose and accustom the gastrointestinal tract of the patient to its presence; when this is done, the dose can gradually be raised to the optimal dosage. Recently, **ferrous salts** have been advocated as being superior in absorptive power and necessitating smaller doses of material. The reviewer has compared a ferrous compound with reduced iron and ferric and ammonium citrate and has found it to be at least as effective (*Ibid*). H. W. Fullerton (Edinburgh M. J. 41: 99 (Feb.) 1934) used **ferrous sulphate** and found that a small dose of the dried salt (0.8 Gm -12½ grains) was as effective in hemoglobin regeneration as 6.0 Gm (1½ drams) of ferric ammonium citrate. The reviewer has pointed out in the above publications that most cases of hypochromic anemia will respond when adequate dosage of iron is given, but that an occasional case which is refractory responds when copper in the form of **copper sulphate** 0.006 Gm (1/10 grain) is added to the daily iron ration. It is probably inadvisable to use copper except in the occasional refractory case, since chronic copper poisoning with possible hemochromatosis may result.

(Organic compounds of iron are probably of little or no value, certainly as compared with the inorganic preparations. This is brought out in the experiments of C. A. Elvehjem, E. B. Hart, and W. C. Sherman (J. Biol. Chem. 103: 61 (Nov.) 1933). A. J. Patek, Jr., and G. R. Minot (Am. J. M. Sc. 188: 206 (Aug.) 1934) made the interesting observation that concentrated **bile pigment** alone might increase the hemoglobin or might facilitate the absorption or utilization of iron. One patient, unable to obtain a normal hemoglobin level with large doses of iron, increased her hemoglobin concentration when bile pigment was administered in addition to the iron.

**OTHER TYPES OF ANEMIA.—Aplastic Anemia.** W. P. Thompson, M. N. Richter and K. S. Edsall (Am. J. M. Sc. 187: 77 (Jan.) 1934) found, on analyzing a group of cases of aplastic anemia, that many discrepancies were present between the text-book description of the classical case and their cases as observed at the bedside. (This is probably true for many conditions.) They found that evidences of regeneration were frequently present. (On the other hand, careful analysis of their cases show that certain of them were, in all likelihood, examples of aleukemic leukosis (*q. v.*)). W. Dameshek (New England J. Med. 210: 687 (Mar. 29) 1934) stated that although certain idiopathic cases of aplastic anemia are still encountered, the great majority present a more or less well-defined history of contact with a chemical such as benzol, arsenic, arsphenamine, neoarsphenamine, radium, radio-active substances, mesothorium in watch-dial workers, x-rays, and gold. This author reported a case following the use of large amounts of gold sodium thiosulphate in the treatment of lupus erythematosus. There has been no advance in therapy in this disease, the custom being to give numerous **transfusions** until further evidence of blood regeneration is lacking. R. Gottlieb (Ann. Int. Med. 7: 895 (Jan.) 1934) recommends trial of **splenectomy** and cites a case in which a remission occurred lasting for 2 months.



***Congenital Hemolytic Anemia.***—The most striking advance in this disease has been the discovery that the fundamental abnormality is an increased tendency of the red blood cells to assume a spherical shape. Otto Naegeli (“Blutkrankheiten und Blutdiagnostik” 5th Edit, Julius Springer, Berlin, 1931) and R. L. Haden (Am. J. M. Sc 188: 441 (Oct.) 1934) designate this tendency as spherocytosis. This abnormality was discovered by comparing the average red blood cell diameter which is always less than normal (microcytosis) with the average corpuscular volume, which may be normal or even increased. This can only be due to an increased thickness of the red cells, which Haden and Naegeli feel is an inborn error in the disease, as much of an anatomical variation as the “tower” skull and other physical abnormalities often present. Haden found that the increased fragility (the amount of dilution necessary to produce hemolysis) varied directly with the degree of spherocytosis or altered shape of the cells, and stated that “the cells in this disease may be regarded as nearer the hemolysis point by reason of their shape” He concludes that “the one fundamental variation from normal is the microspherocytosis. The anemia, jaundice, splenomegaly, reticulocytosis and increased fragility are all secondary to the globular form of the erythrocyte.”

As regards *treatment*, E. C. Reifenshtein and E. G. Allen (J. A. M. A 103 1668 (Dec 1) 1934) recommend, on the basis of 3 cases, the use of **parenteral liver extract**, particularly in the mild case of the disorder. Their 3 cases all showed definite clinical improvement. Other observers disagree with this concept, however, maintaining that not only may hemoclastic crises appear, but that the gall-bladder and liver may become irretrievably damaged before **splenectomy** is finally done.

***Ovalocytosis, Sicklemia, Sickle Cell Anemia.***—L. H. Pollock and W. Dameshek (Am J M. Sc. 188 822 (Dec ) 1934), in describing elongation of the red blood cells in a Jewish family, review the often confusing terms which have arisen about this curious disorder. “Ovalocytosis” is said to be present when 10 per cent or more of the red cells are oval in shape. Elongation is the next degree abnormality. When sickled red cells are present without anemia, “sicklemia” is said to be present. An anemia in which sickled cells predominate is called “sickle cell anemia.” Oval-shaped and elongated red blood cells have now been frequently reported in members of the white race, although sickle cell anemia has so far been described only in the colored. Pollock and Dameshek state that “it is probable that oval, elongated and sickled red cells and sickle cell anemia represent various gradations in the same general abnormality of red blood cells.” The disorder is fundamentally an hereditary one, and probably of no significance unless severe anemia is present. L. W. Diggs, C. F. Ahmann and J. Bibb (Ann Int Med 7 769 (Dec ) 1933) demonstrated that a tendency of the red cells to sickle could be observed in 83 per cent of 2539 negroes when sealed moist preparations of blood were examined. These authors found that the ratio of sickle cell anemia to the sickle cell trait is about 1 to 40 and that the trait itself has no significance. J. C. Corrigan and L. W. Schiller (New England J Med 210 410 (Feb. 22) 1934) noted the presence in their autopsied case of sickle cell anemia of an extremely small spleen weighing 0.87

Gm. L. W. Diggs (Am. J. M. Sc. 187:521 (Apr) 1934) demonstrated in 7 cases of definite sickle cell anemia the ineffectiveness of liver, liver extract both by mouth and parenterally, desiccated hog's stomach, bone-marrow extract, iron, and transfusions.

**"SPLENIC ANEMIA," BANTI'S DISEASE, ETC.**—In most cases of continued enlargement of the spleen, leukopenia is a prominent feature and there is usually a distinct anemia, together with some reduction in the blood platelets. R. C. Larrabee (Am. J. M. Sc. 188:745 (Dec) 1934) suggested the term "chronic congestive splenomegaly" for this group of cases and pointed out their similarities despite the wide difference in etiological agents. Cirrhosis of the liver, syphilitic splenohematomegaly, chronic malaria, residual splenomegaly following various infections all produce the same clinical state which, by the uncritical, is often called "splenic anemia" or Banti's disease. Whether there is such an entity as Banti's disease is open to question. (Most cases of alleged Banti's disease have, in the reviewer's experience, been finally diagnosed as chronic myelosis.) Increase in the pressure in any part of the portal circuit may result in splenomegaly, gastrointestinal hemorrhages, etc. The mechanism of the leukopenia and slight anemia has not been worked out, although Larrabee suggests a possible diminution in "active principle" because of involvement of the liver.

**Splenectomy** will reduce the pressure in the portal circulation and thus reduce the dangers of hematemesis and ascites. E. Storti (Haematologica 15:107, 1934) and other Italian workers have recently advocated the use of **ligation of the splenic artery** as a simpler and easier technic than splenectomy.

**POLYCYTHEMIA.**—*Etiology*—Two main types are recognized, *i. e.*, the idiopathic (polycythemia vera) and the secondary. The mechanisms involved in the secondary type are well brought out in a case reported by J. J. Waring and W. B. Yegge (Ann. Int. Med. 7:190 (Aug) 1933). This patient had longstanding bronchial asthma and emphysema which undoubtedly produced anoxemia and cyanosis and was followed by polycythemia. The patient was working at a high altitude and this factor alone was sufficient to cause some degree of polycythemia. Possibly the pulmonary artery might have become sclerosed as the result of increase in the pressure within the lesser circuit. All of these factors tended to cause a greatly increased burden upon the heart.

Waring and Yegge (*Ibid.*) discuss "*Ayerza's disease*," the conception of which has greatly changed since Ayerza described his "black cardiacs" in 1901. M. R. Castex, E. L. Capdehourat, and R. L. Repetto (Arch. med. chir. de l'app. respir. 8:385, 1933) discuss the mechanisms in the development of this disease entity of chronic severe cyanosis, and polycythemia. Although they do not minimize the importance of pulmonary artery arteriosclerosis as a factor, they stress the more fundamental factor of various types of chronic bronchopulmonary disorders which produce cyanosis. The individual affected, if his marrow is normal, reacts with polycythemia, a compensatory mechanism. Arteriosclerosis of the pulmonary artery, they feel, is secondary to the chronic bronchopulmonary disease. Heart disease need not necessarily be present. These authors feel that

the reason the syndrome is not seen more frequently is that many older individuals with bronchopulmonary disease do not have sufficiently reactive marrow.

The cause or causes of the so-called true polycythemia have not yet been discovered. R. S. Morris (J. A. M. A. 101:200 (July 15) 1933) came out with an attractively simple hypothesis that the erythremia might be the result of hypersecretion of "addisin" (the so-called gastric hormone) or of hypersusceptibility of the marrow to it. He attempted to contrast pernicious anemia (due to a deficiency in "addisin") with polycythemia ("hyperaddisinism"). Unfortunately, these hypotheses have not stood the test of even a single year of investigation (*cf.* also under ETIOLOGY OF ANEMIA). (Paul Reznikoff, N. C. Foot, J. M. Bethea, and E. F. DuBois (Tr. A. Am. Physicians 49:273, 1934) demonstrated that the blood-vessels of the marrow in cases of the idiopathic type of polycythemia showed unusual changes of the intima and media. These circulatory changes might be the initial factor which caused a great increase in the anoxemia of the marrow with resultant polycythemia. This author also pointed out that the disease was much more common among the Jewish population of New York City than in other groups and suggested an hereditary factor. H. W. Boyd (Am J. M. Sc 187:589 (May) 1934) describes a case characterized by polycythemia, duodenal ulcer, coronary thrombosis, and ascites and discusses the possibility that the ulcer might have had some bearing on the production of polycythemia; he feels, however, that the polycythemia was probably instrumental in causing the duodenal ulceration. A. Baserga (Policlinico (Sez. med.) 41 17, (Jan.) 1934) pointed out that polycythemia is occasionally associated with primary disease of the central nervous system particularly in the diencephalo-hypophyseal region (acromegaly, encephalitis lethargica) and reported a case in which polycythemia was present in a case of pituitary neoplasm. It is possible that a red cell regulating mechanism is situated in the hypothalamic pituitary portion of the brain.

**Diagnosis.**—Most cases of polycythemia vera probably go unrecognized and are diagnosed as heart disease, angina pectoris, cerebral disease, peripheral vascular disease, etc. The reviewer has had occasion many times to comment on this fact. The infrequency with which routine erythrocyte counts are done and the inaccuracy of the Tallqvist hemoglobin test account to a great extent for this state of affairs, which cannot be corrected unless the possibility is borne in mind that the disease might be present and a red cell count is made. The possibility should be considered in a patient with a dusky cyanotic appearance presenting vague symptoms which are frequently cerebral in type, at times circulatory. L. H. Sloan (Arch. Neurol. and Psychiat. 30 154 (July) 1933) states that the disease has predominantly a nervous and mental symptomatology. This may easily be understood, since the blood volume is increased, the cerebral vessels distended, the circulation slowed, and the viscosity of the blood increased. P. Schiff and R. Simon (Ann. méd. psychol. 91 616 (May) 1933) describe a case characterized by cataplexia, chorea, and mental confusion. K. Bieling (Med. Klin. 29 1410 (Oct. 13) 1933) describes a severe case of Ménière's syndrome due to polycythemia.

It is important for the practicing physician to be on the lookout for these cases, because much may be done with appropriate treatment

**Treatment.**—There has been no improvement in the fundamental treatment of polycythemia. E. H. Falconer (Ann Int Med 7 172 (Aug) 1933) suggests the use of **venesection** as an adjuvant to the use of **phenylhydrazine hydrochloride**. The reviewer has repeatedly used this method and finds it of value. If the erythrocyte count is 8 to 10 million per c mm, it is probably best to begin by removing from 500 to 1000 c c of blood and to begin phenylhydrazine therapy only when the red cell count is about 6.5 million. This procedure avoids excessive hemolysis and possible thrombotic complications which might ensue if large doses of phenylhydrazine were given immediately. Phenylhydrazine hydrochloride may be given either in capsules of 0.03 Gm ( $\frac{1}{2}$  grain) or dissolved in aqueous solution (1 dram to  $\frac{1}{2}$  gram). The original dosage is usually 0.09 to 0.15 Gm. ( $1\frac{1}{2}$  to  $2\frac{1}{2}$  grains) daily, which is diminished to a maintenance dose of about 0.03 Gm ( $\frac{1}{2}$  grain) daily, depending upon the individual patient. It is difficult to gauge the exact dosage, which must be individually adjusted. H. Vaquez and M. Mouquin (Presse méd 42 1065 (July 4) 1934) also discuss the treatment of the disease with phenylhydrazine. They begin with a dosage of 0.05 to 0.1 Gm ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) and suspend medication in any event when the patient has taken a total of 3 Gm ( $\frac{3}{4}$  dram). They discuss the possible complications such as thromboses and the rare examples of permanent cure. E. H. Falconer (J A M A 101 1633 (Nov 18) 1933) reports a case in which a remission has been present for 11 years following treatment with phenylhydrazine. C. T. Stone, T. H. Harris and M. Bodansky (Ibid 101 495 (Aug 12) 1933) are convinced that **acetylphenylhydrazine** is less toxic and provides a greater margin of safety in cases of overdosage; in 2 cases these authors were able to maintain a normal red cell count with only 100 mgs ( $1\frac{1}{2}$  grams) weekly. The status of the various methods of treatment including that by x-ray treatment over the bones is discussed in a review of the subject (Am J M Sc 187 716 (May) 1934). **Phenylhydrazine** easily holds first rank.

**LEUKOSIS (LEUKEMIA).—Classification.**—W. Dameshek, in a recent review (New England J Med 210 531 (Mar 8) 1934) states that there are 3 types of white blood cells: (1) the granulocytes, (2) the lymphocytes, and (3) the monocytes. These owe their origin in the blood stream to 3 separate sources: (1) the bone-marrow, (2) the lymphoid tissue, and (3) the reticuloendothelial system. Leukemia might be better termed "leukosis," since it represents pathologically a generalized proliferation of the various types of white blood cells. Since 3 types of white blood cells and 3 separate blood-forming organs are present, 3 types of leukosis are possible: myelosis, lymphadenosis, and reticulosis.

The existence of *monocytic leukemia*, a third type of leukosis originating in the reticuloendothelial system, has been abundantly confirmed since W. Dameshek's report of 1930 (Arch Int. Med 46 718 (Oct) 1930). A. Levine (Folia hæmat. 52:305, 1934), who reports 9 cases, found that the disease was relatively common. The disease is called reticuloendotheliosis by several authors. R. Gittins (Arch. Dis. Childhood 8. 367 (Dec.) 1933) gives an excellent review

of the subject together with a classification of the various types of reticuloendothelial proliferations. He groups them as (A) *Reactive* (to blood destruction, sepsis, chemical abnormalities), (B) *Focal Neoplastic* (Reticuloma, etc.), and (C) *Leukotic* (Reticuloendothelial leukosis or monocytic leukemia, leukemic and aleukemic). A. G. Foord, L. Parsons and E. M. Butt (J. A. M. A. 101:1859 (Dec 9) 1933) who report four cases of "leukemic reticuloendotheliosis" also follow much the same type of classification. G. R. Callender (Am. J. Path. 10:443 (July) 1934) in his review of the classification of the various types of leukocytic proliferation uses the term "Reticulocytoma, Leukemic." Most of these classifications, particularly those relating to reticuloendothelial proliferations, are similar to those which have been published in European articles. The most comprehensive of these is that one of A. Baserga (Hæmatologica II Recen 4:61, 1933).

The leukoses may be considered to be generalized proliferations of one of the white cell forming tissues. W. Dameshek (New England J Med 210:531 (Mar. 8) 1934) states that this proliferation may be associated with large numbers of circulating leukocytes or even with great diminution in their number. "Aleukemic leukemia," being a paradoxical term, is best replaced by using the terms *aleukemic myelosis*, *lymphadenosis*, and *reticulosis*. The fundamental pathological process is identical in both the aleukemic and the leukemic forms.

**Etiology.**—The great majority of observers have finally agreed, after years of bickering, that the leukoses represent generalized neoplastic proliferations of one of the white blood cell forming tissues. This concept has recently received confirmation in the experimental laboratory at the hands of J. Furth, H. R. Seibold, and R. R. Rathbone (Am J Cancer 19:521 (Nov.) 1933) and of W. Bungeler (Klin Wchnschr 11:1982 (Nov 26) 1932; J. A. M. A 102:1086 (Mar 31) 1934). Both of these groups of investigators were able to induce leukosis in mice. The leukemic and sarcomatous lesions were frequently present together in the same mouse and transitions between one and the other state could often be seen. These lesions, leukemic or sarcomatous, corresponded chemically and biologically to those of malignant tumors. J. Furth (J. Exper Med 58:253 (Sept) 1933) was also able to induce leukosis in chickens by means of injection of material free from viable cells. The "acute" leukoses, although resembling so closely severe infectious processes, should be regarded as highly malignant lesions composed of exceedingly primitive mesenchymal cells.

**Diagnosis.**—Among the most frequently misdiagnosed conditions in hematologic practice are the aleukemic leukoses. C. W. Baldrige and W. M. Fowler (Arch Int Med 52:852 (Dec.) 1933) state that 5 per cent of their cases of diffuse myelosis were permanently aleukemic. Their statement that "most physicians seem to regard aleukemic myelosis as an obscure form of hematopoietic disease which can be diagnosed only at necropsy" is heartily endorsed by the reviewer. W. Dameshek states (New England J Med 210:531 (Mar 8) 1934) that in his experience with cases of leukemia, *the great majority are aleukemic*. These cases usually present themselves with anemia. In the aleukemic myeloid types, splenomegaly is the outstanding feature. Because of this, Banti's disease or splenic anemia is frequently diagnosed. In the lymphatic types generalized

lymphadenopathy is almost always present; in the monocytic type lymphadenopathy and splenomegaly are only slight in degree. All types are associated with moderate or severe anemia, leukopenia or a normal white blood cell count, and thrombocytopenia. The anemia is frequently macrocytic in type and pernicious anemia is often diagnosed. Because the leukocyte count is low, agranulocytosis may be considered. In the presence of ecchymoses and bleeding, the diagnosis of purpura hemorrhagica is frequently made. The reduction in red blood cells, white blood cells, and in platelets, suggests a "destructive" process of the bone-marrow which is indeed borne out by bone-marrow biopsy. This diagnostic method has proved exceedingly helpful in the ultimate solution of these often very puzzling cases. In any case of obscure, longstanding anemia, the possibility of one of the aleukemic leukoses should be strongly considered.

The acute leukoses, when aleukemic, are, peculiarly enough, to be differentiated from agranulocytosis. Many cases of so-called agranulocytosis are in all probability examples of acute leukosis. This view was stated by W. Dameshek (J. A. M. A. 102:950 (Mar. 24) 1934), who cited some of the diagnostic features, chief among which was the progressive anemia and reduction in platelets present in the leukotic process. H. Jackson (Am. J. M. Sc. 188:604 (Nov.) 1934) also cites these features and makes this epigrammatic statement: "Leukemia is still leukemia whether the white count be 50 or 50,000 per c. mm." He stresses the value of the bone-marrow biopsy.

M. M. Strumia (*Ibid.* 187:826 (June) 1934) points out the transitions which may develop from extreme leukopenia to extreme leukemia in cases of leukosis. He goes too far, it appears, in attempting to link up the two conditions as being pathogenetically similar. The elevation in basal metabolic rate which frequently occurs in the chronic types of leukosis may be so striking at times as to suggest the possibility of hyperthyroidism. W. Dameshek, D. D. Berlin, and H. L. Blumgart (New England J. Med. 210:723 (Apr. 5) 1934) comment upon this possibility and its possible implications. (See under TRIANGULAR.)

The diagnosis of the type of leukemia is relatively simple in the chronic varieties of the disease, but becomes difficult in the fulminating acute varieties, when a primitive type of blood cell formation is taking place and extremely young cells are present in the circulation. C. E. Forkner (Arch. Int. Med. 53:1 (Jan.) 1934) takes up the diagnostic points by which the primitive cells (myeloblasts, lymphoblasts, monoblasts) may be diagnosed in a given case. In common with other authors, he states that the supravital technic is of particular value in the differentiation of the monocytic strain of cells, although in certain cases it is only by a combination of all the available methods of study (including that of oxidase staining) that an acceptable opinion concerning the cell type may be established. It is his opinion that the clinical picture of diffuse marked swelling of the mucous membranes, particularly of the gingivæ, usually associated with ulceration and necrosis, is characteristic of *acute monocytic leukemia* and usually absent in the other types. To this opinion, the reviewer can only partially subscribe, since the lymphatic type sometimes gives very striking gingival and buccal lesions.

The *heterophile antibody test*, introduced in the diagnosis of benign lymphadenosis ("infectious mononucleosis") *q. v.*, has been utilized by A. Bernstein (J. Clin. Investigation 13:677 (July) 1934) in the diagnosis of leukemia. This author found that heterophile agglutinins in the blood sera of 21 patients with leukemia were confined to low titers (less than 1 to 4) in 20 instances; whereas in most of the conditions simulating leukemia, heterophile agglutinins were found over a wider distribution of titer, up to 1 to 16. Bernstein brings out that the mechanism whereby antibodies are formed is disturbed in leukemia.

**Treatment.**—The treatment of the leukoses continues to be unsatisfactory, although a patient with the chronic form may frequently be tided along for a number of years. L. F. Craver (M. Clin. North America 18:703, 1934) gives in detail the plan of treatment for chronic myelosis in use at the Memorial Hospital, New York. Equal daily doses of **x-rays** are given **over the spleen** to total a mild erythema dose (about 600 "r"). The cycle of treatment is finished in about a week and no further treatment for from 3 months to a year is necessary. The **bones** are also **irradiated**, the proximal ends of the long bones, the spine and the sternum being selected. Craver also cites his experience with **arsenic (Fowler's solution)** and believes it to be of value between cycles of x-ray treatment (It is also of value when proper x-ray treatment is not readily obtainable). He uses more guarded doses than those suggested by Forkner, in 1930, and begins with 3 minims (0.2 cc) 3 times daily, raising the dosage by 1 minim (0.06 cc) per dose daily until the patient is taking about 10 minims (0.6 cc) 3 times daily. (When x-rays are not being used, this dosage may be inadequate. It should be controlled by frequent leukocyte counts.) U. J. Portmann (J. A. M. A. 102:178 (Jan. 20) 1934) states that chronic myelosis is ultimately a generalized disease, and that certain organs are affected in greater degree than others. Treatment by **x-rays** should, therefore, be individualized and should always be administered to the vertebræ, the ribs, and the sternum, at times to the long bones. In the treatment of chronic lymphadenosis (lymphatic leukemia) Craver discusses very carefully the procedure of treatment by x-ray, depending to great part upon the regions involved, the leukocyte count, the patient's condition, and the metabolic rate. Cycles of treatment are given over the affected lymph-nodes and possibly over the mediastinal and retroperitoneal areas, if the patient's condition permits.

Because of the extreme elevation in basal metabolic rate which is so striking a manifestation of certain cases of chronic leukosis, particularly of the lymphoid type, W. Dameshek, D. D. Berlin, and H. L. Blumgart (*loc. cit.*) conceived the idea that **thyroidectomy** might be of benefit. These authors point out that many of the symptoms of the disease (increased sweating, tachycardia, reaction to cold, etc.) may be part of the hypermetabolism rather than due directly to the leukotic process. In 1 case of aleukemic lymphadenosis with a metabolic rate of +65 per cent, there was striking relief to all the symptoms followed by complete regression of all the lymph-nodes and the spleen. The blood-picture became normal. This remission has persisted for 1½ years. The authors state that the procedure is worthy of further trial in similar cases.

There has been no advance in the treatment of the acute leukoses.

**TUMORS OF WHITE BLOOD CELLS.—Classification.**—G. R. Calender (Am J. Path 10:443 (July) 1934), the Registrar of the American Registry of Pathology, gives the following “semi-official” classification of tumors of the white blood cells. lymphosarcoma myelosarcoma, and reticulum cell sarcoma These may be leukemic and aleukemic. Hodgkin’s disease is grouped among the reticulum cell proliferations The reviewer has used much the same classification, although he has subdivided the neoplasms a little further, chiefly according to the degree of cellular maturity Thus, the generic terms for tumors of the lymphoid, myeloid, and reticulum cells (histiocytes) are myeloblastoma, lymphoblastoma, and histiocytoma Lymphoblastoma is subdivided into lymphosarcoma (highly malignant) and lymphoma (relatively benign) Myeloblastoma (commonly called chloroma) is subdivided into myelosarcoma and myeloma (“Multiple myeloma” is a lymphoid tumor composed of plasma cells and should be called plasmoma) Histiocytoma is subdivided into reticulum cell sarcoma and reticuloendothelioma Any of these forms, particularly of the more malignant types, may, by metastasizing into the blood stream, produce the picture of leukosis

**Differential Diagnosis.**—The differential diagnosis of enlarged lymph-nodes is frequently very difficult I W Held and A A Goldbloom (M Clin North America 18 633, 1934) discuss a few of the differentiating points, but the reviewer has often found it difficult to distinguish between a pyogenic, tuberculous, carcinomatous, and lymphosarcomatous process by inspection and palpation The diagnostic procedures which should be done in a given case are, besides physical examination, leukocyte count, differential count of the white cells, tuberculin test, x-ray of the chest, possibly basal metabolic rate determination In a questionable instance, and even when the diagnosis appears obvious, it is imperative to perform a biopsy of one of the affected nodes This procedure is of more value than all the possible physical examinations and laboratory tests that may be done

**Treatment** Craver (*loc. cit*) reviews very carefully and very sanely the therapy of the *malignant tumors* of the white cells He states that the fundamental plan of treatment is determined by asking the question as to whether the disease is localized and therefore offers some hope of cure, or whether it has spread so far beyond its source that treatment must be only palliative T Leucutia (Am J M Sc 188 612 (Nov) 1934) says that **radiation therapy** must be considered the method *par excellence* in the treatment of lymphosarcoma Thorough radiation therapy increases the expectation of life in all forms of lymphosarcoma from  $2\frac{1}{2}$  to  $3\frac{1}{2}$  years and leads to cure in at least 10 to 15 per cent of the cases (This is not the reviewer’s experience, he is much more pessimistic) Leucutia believes that it is essential to radiate the entire lymphatic system, regardless of whether the disease is localized or generalized This causes “depletion of the blood” and requires careful management He states that this drastic procedure leads at times to complete eradication of the disease, the outlook for the individual patient varying with the primitiveness of the cell, and the extent of involvement at the time of treatment Anemia, cachexia, and fever usually render prognosis unfavorable.



**HODGKIN'S DISEASE.**—The tendency in recent years has been to group Hodgkin's disease among the proliferative lesions arising from the reticuloendothelial (monocytic) cells. Callender (*loc. cit.*) follows this grouping and it has been used by the reviewer (*Folia hæmat.* 49:64, 1933). The disorder may be localized or generalized. If generalized, involving the lymph-nodes, spleen, liver, and bone-marrow, it may be said to be leukotic, and the reviewer described a case of this sort as "aleukemic reticulosis" (*Folia hæmat. loc cit*). The most comprehensive review of the disease which has appeared in recent years is that of A. Wallhauser (*Arch Path.* 16:522 (Oct); 672 (Nov.) 1933). This author takes up in great detail the many investigations which have been made in the attempt to show that the disease is of infectious (particularly tuberculous) origin. He does not appear to be enthusiastic about this possibility and this feeling is shared by most investigators: *viz.*, that Hodgkin's disease is not of infectious origin, but definitely neoplastic in type.

*Diagnosis* cannot be made by the blood picture, which varies tremendously, according to the stage and type of the disease. It is true that the blood-picture shows more or less characteristic changes (provided the diagnosis is known beforehand). Biopsy must be resorted to, and its importance cannot be over-emphasized. R. F. Ogilvie and C. E. van Rooyen (*J. A. M. A.* 102:1842 (June 2) 1934) report on the *Gordon test*, which consists in injecting into the brains of rabbits some of the lymphoid material suspended in saline (after it has remained in the ice-box for about a week). If the test is positive for Hodgkin's disease, the rabbits develop severe ataxia, incoordination, paralysis of the hind legs, and death. These authors found the test of value in 2 clinical cases. It needs further trial before its exact value can be demonstrated.

The *treatment* of Hodgkin's disease is persistent **x-ray therapy**, and this is commented upon by Craver, Leucutia and Wallhauser (all cited above). Leucutia (*Am J. M. Sc.* 188:612 (Nov.) 1934) states that radiation therapy increases the expectancy of life, and produces 5- and 10-year survivals in about one-third of the cases. This author uses very drastic treatment covering the entire lymphoid system.

**BENIGN INFECTIOUS LYMPHADENOSIS (INFECTIOUS MONONUCLEOSIS, GLANDULAR FEVER.**—*Nomenclature.*—The term "infectious mononucleosis," suggested in 1922 by Sprunt and Evans and Longcope, is an unfortunate one, since the cells concerned are not monocytes but lymphocytes; again, how can a mononucleosis be infectious? Pfeiffer, in 1885, described a group of cases in children which he called *glandular fever*, and this is by far a better term since it is noncommittal and clinically descriptive. Benign infectious lymphadenosis, although rather unwieldy, describes accurately the pathological process which is that of intense proliferation of lymphoid cells, a proliferation, however, which is benign (*i. e.*, not leukemic or sarcomatous) and infectious in origin.

*Etiology.*—The infectious nature of the disease is well known. F. Penati (*Minerva med.* 1:414 (Mar. 31) 1934) in his comprehensive article, analyzes the various experiments which have been performed in an attempt to determine a specific etiological agent. The most promising results, he states, are those of

Aage Nyfeldt, who isolated a bacterium from the blood-stream identical morphologically and culturally with that isolated by Murray, Webb and Swann from a highly contagious disease of rabbits associated with monocytosis Nyfeldt called this organism *Bacterium monocytogenes hominis*.

Many authors have commented upon the frequency of the disorder in medical students, nurses, physicians, and members of physicians' families. E. Schulz (München med. Wchnschr. 80. 1809 (Nov. 17) 1933) had the unusual opportunity of observing an epidemic of the disease and was thus able to draw some inference regarding the incubation period, which he concluded was 1 week or less.

**Pathology.**—The pathology of the disease has been but little studied, since it is so benign a disorder and complications are so few. Penati (*loc. cit.*) describes the intense lymphoblastic hyperplasia which the reviewer has found exceedingly difficult to differentiate from the lymphoblastic proliferation of lymphosarcoma or of malignant lymphadenosis (leukemia).

**Symptoms.**—Schulz (*loc. cit.*) was able to study 35 cases in an epidemic of the disease. Great fatigue and moodiness, particularly in children, usher in the disease and are soon followed by conjunctivitis, at times epistaxis, and at times vomiting. Headache develops and becomes quite severe at times. The lymph-nodes become enlarged and are the characteristic feature of the disorder. Schulz states that they are frequently overlooked by the physician, and to this the reviewer emphatically subscribes. The nodes are frequently tender. The spleen is usually enlarged.

**Blood Picture.**—All recent observers are agreed that the blood picture is that of a well-marked lymphocytosis with the presence of all types of abnormal lymphocytes. C. A. Stuart, A. M. Burgess, H. A. Lawson, and H. E. Wellman (Arch. Int. Med. 54: 199 (Aug.) 1934) describe carefully the cytologic changes and state that all gradations in type between the small normal lymphocyte and the lymphoblast are seen. Most striking features are the vacuolated cytoplasm, often with irregular projections from the surface of the cell, the nucleus is frequently indented. The presence of all types of immature lymphocytes is properly stressed by these authors, who were also able to observe anitotic division of the lymphocytes in the peripheral blood. Penati (*loc. cit.*) describes the lymphocytes and their many types very carefully; in other papers, this author, together with Levi (Hæmatologica 15, 1934), describes the lymphocytes and monocytes in the experimental infectious lymphadenosis of rabbits. It is the reviewer's opinion that the large lymphocytes of glandular fever may easily be differentiated from monocytes if the various characteristics of cytoplasm, granules in the cytoplasm, types of nucleus, character of nuclear chromatin, etc., are all kept in mind. The large lymphocyte has a sky-blue, pale-blue, or deep-blue cytoplasm which is clear, with only a few large granules, if any, the nucleus is only about one-half the size of the cell, round usually, and is made up of heavy chromatin blocks. The monocyte is gray-blue in color, with many fine granules in the cytoplasm, the nucleus is large in comparison to the size of the cell, usually indented and composed of a fine chromatin mesh. Further differentiation may be made from supravital studies (*q. v.*).

**Diagnosis.**—Most of the cases, being mild, escape recognition through failure of the attending physician to palpate carefully for enlarged lymph-nodes. The recognition of the disease among physicians and their associates is possibly due to the fact that a blood smear is apt to be made. The blood picture is the most important diagnostic feature. The extreme lymphocytosis with so many immature lymphocytes suggests acute lymphatic leukemia, but this is ruled out by the course and the absence of anemia and reduction in blood platelets. Recently, a new and interesting diagnostic test has been introduced. Described originally by Paul and Bunnell in 1932, the heterophile agglutination test has received abundant confirmation. A. Bernstein (J. Clin. Investigation 13:419 (May) 1934) describes the technic and points out the diagnostic importance of agglutination of sheep's cells by the patient's serum in high titers. The details of the technic from an immunologist's standpoint have been investigated by Stuart in a paper by Stuart, Burgess, Lawson, and Wellman (*loc. cit.*). Stuart states that the presence of agglutinins for sheep erythrocytes in human blood was until recently of only academic interest. In glandular fever, these agglutinins become greatly increased so that positive agglutination may occur in as high a dilution as 1:5120. A suspension of sheep's cells is added to successive dilutions of the patient's blood serum and after incubation for a few hours, after a stay in the icebox over night, the results are read. Stuart states that "with substantiating clinical and cytologic pictures, serum agglutinins in dilutions of 1:320 or more may well be considered positive." A. C. Van Ravenswaay (New England J. Med. 211:1001 (Nov. 29) 1934) considers the test positive when complete agglutination occurs at a dilution of 1:32, but other authors (Bunnell, Bernstein) consider even 1:8 and 1:16 as positive results.

N. Rosenthal and G. Wenkebach (Klin. Wchnschr. 12:499 (Apr. 1) 1933) state that those cases showing the clinical and hematological features of "infectious mononucleosis," but with a negative agglutination test, are examples of "glandular fever" and to be differentiated from true "infectious mononucleosis." To this view, the reviewer does not subscribe; possibly the agglutination test does not always give the correct information. It must be remembered, as van Ravenswaay points out, that the test is nonspecific, like the Weil-Felix test in typhus fever, which too may frequently be negative despite the typical features of the disease being present. It is comforting, in a case which suggests acute lymphatic leukemia, to obtain a positive agglutination test in high titer. A. Bernstein (J. Clin. Investigation 13:677 (July) 1934) points out that in leukemia, the titers are exceedingly low. The cause for the increased tendency on the part of the blood serum in the disease to agglutinate sheep's red cells has not as yet been worked out.

**Treatment.**—No treatment except that of the symptomatic variety is ordinarily required.

**AGRANULOCYTOSIS (GRANULOCYTOPENIA, GRANULOPENIA, MALIGNANT NEUTROPENIA).—Etiology.**—Much speculation has taken place regarding the sudden prominence of agranulocytosis as a clinical entity. Its etiology was a mystery. R. R. Kracke and F. Parker (J. Lab. and Clin. Med. 19:799 (May) 1934) list the following agents which had been

at one time or another suspected - live bacteria, dead bacteria, hormonal products, radiation, and chemicals. None of these agents had been consistently implicated. Almost simultaneously, however, a group of articles appeared in which the etiology of the disease could be quite clearly traced to the use of a drug or drugs. C. H. Watkins, in a short note (Proc Staff Meet Mayo Clin. 8:713 (Nov. 22) 1933), implicated the barbiturates. F. W. Madison and T. L. Squier (J. A. M. A. 102:755 (Mar. 10) 1934) were able to show quite conclusively in 14 cases that amidopyrine and drugs containing amidopyrine had been used prior to the attack of agranulocytosis in all of their cases, they were also able to reproduce the disease in 2 instances by giving the drug experimentally. A. M. Hoffman, E. M. Butt, and N. G. Hickey (*Ibid.* 102:1213 (Apr. 14) 1934), in re-investigating their 14 cases of agranulocytosis, demonstrated that all of them but one had taken amidopyrine prior to development of the disease, one had taken dinitrophenol. W. B. Rawls (Am. J. M. Sc. 187:837 (June) 1934), C. Holten, H. E. Nielsen, and K. Transbøl (Ugeskr. f. læger 96:155 (Feb. 8) 1934), J. E. Benjamin and J. B. Biederman (J. A. M. A. 103:161 (July 21) 1934) and others, reported clear-cut instances of the disease following the ingestion of amidopyrine. Aspirin and the barbiturates appeared to be of no etiological importance. W. Dameshek and S. L. Gargill (New England J. Med. 211:440 (Sept. 6) 1934), S. S. Bohm (J. A. M. A. 103:249 (July 28) 1934) and S. Silver (*Ibid.* 103:1058 (Oct. 6) 1934) showed that dinitrophenol -the drug so widely-heralded in the treatment of obesity- had almost certainly brought about the disease in their cases.

R. R. Kracke and F. P. Parker (*loc. cit.*), in analyzing chemically the various drugs which had been implicated (neoarsphenamine, arsphenamine, acetamid, phenacetine, and amidopyrine) showed that they were all distinguished by the presence of a benzene ring with an  $\text{NH}_2$  (amino) linkage, they therefore called the offending chemicals the "benzamine drugs." These authors postulated that the oxidation products of these drugs affected the bone-marrow causing the disease (Am. J. Clin. Path. 4:453 (Nov.) 1934). The rapid onset of granulocytopenia following a small dose of amidopyrine suggested to J. E. Benjamin and J. B. Biederman (*loc. cit.*) that a hypersensitivity to the drug was present. This is, of course, borne out by the small number of actual cases of the disease in contrast to the millions of administrations of amidopyrine and other drugs, as noted by Paul Reznikoff in the Special Report of the Council on Pharmacy and Chemistry (J. A. M. A. 102:2183 (June 30) 1934). The exact mechanism of this possible hypersensitivity has not yet been worked out. It can be stated definitely at present that amidopyrine is a potentially dangerous drug and that a certain few patients are unusually sensitive to even small doses. The unusually large number of sedatives containing amidopyrine in combination would suggest exceedingly great caution in their use. H. Jackson (Am. J. M. Sc. 188:482 (Oct.) 1934) points out that the evidence for the incrimination of the above drugs is not altogether conclusive and multiple factors may be present.

**Pathology.**—There is as yet no unanimity of opinion regarding the essential bone-marrow pathology of the disease, despite the number of autopsies which have been performed. The most careful of recent studies have been made by

R. H. Jaffé (Arch. Path. 16:611 (Nov.) 1933), who agrees with T. Fitz-Hugh, Jr., and E. B. Krumbhaar (Am. J. M. Sc. 183:104 (Jan.) 1932) that the most probable condition which exists is that of "maturation arrest," *i. e.*, a condition in which mature polymorphonuclear cells in the marrow are not formed, although large numbers of primitive cells (myeloblasts and myelocytes) are present. M. M. Strumia (*Ibid.* 187:826 (June) 1934) points out the same thing, although he appears to go too far in attempting to bring leukemia into the same essential disease pattern as agranulocytosis, the difference he says being "a release which occurs in acute leukemias but not in agranulocytosis."

**Diagnosis.**—Many uncritical observers diagnose as agranulocytosis almost any condition in which severe leukopenia is present. C. A. Doan (J. A. M. A. 101:2075 (Dec. 23) 1933) brings out that only 20 per cent. of the cases referred to his clinic with leukopenia are instances of true agranulocytosis. W. Dameshek (*Ibid.* 102:950 (Mar. 24) 1934) points out that many cases of so-called agranulocytosis are in all probability examples of aleukemic leukosis. This has been voiced by H. Jackson (Am. J. M. Sc. 188:604 (Nov.) 1934). W. Dameshek has stated (New England J. Med. 211:440 (Sept. 6) 1934) that the disease is a "selective" one, involving only the bone-marrow leukocytes; the red cells and the platelets not being affected. In any case in which anemia is striking or the hemorrhagic tendency pronounced, the likelihood that agranulocytosis is being dealt with is remote. Pronounced constitutional symptoms in the presence of slight mucous membrane or throat signs, together with severe leukopenia (the red cells and platelets being essentially normal), are enough to suspect the presence of agranulocytosis. In most cases the count is below 2000 per c. mm. (usually below 1000 per c. mm.), and the polymorphonuclear cells are conspicuous by their absence.

**Treatment.**—Up to the present time, the following methods of treatment for the disease have been advocated: **nonspecific therapy, transfusion of blood**, "stimulating" doses of **x-ray**, **nucleic acid** derivatives (pentose nucleotides, adenine sulphate, "leukocytic cream") and **liver extract**. Paul Reznikoff (J. Clin. Investigation 12:45, (Jan.) 1933) obtained good results with the use of **adenine sulphate** in 11 of 15 cases. The drug is obtained from the Eastman Kodak Company in 5-gram ( $1\frac{1}{4}$  dram) lots. It is dissolved in 1 Gm. (15 gram) doses in 50 to 100 c.c. ( $1\frac{1}{2}$  to  $3\frac{1}{3}$  ounces) of sterile salt solution with the use of heat (even boiling) and given slowly intravenously in daily or twice daily injections; reactions are rare. W. Dameshek (New England J. Med. 209:1054 (Nov. 23) 1933; J. A. M. A. 102:950 (Mar. 24) 1934) reports on its successful use without reactions in 7 successive cases. Jackson's **pentose nucleotides** ("**Pentnucleotide N. N. R.**") have been used by many authors with good success. It is given in 10 to 20 c.c. ( $2\frac{1}{2}$  to 5 drams) doses intramuscularly twice daily. 40 c.c. ( $1\frac{1}{3}$  ounces) may be given and the intravenous route may be used. W. Dameshek (New England J. Med. 209:1054 (Nov. 23) 1933) reports severe reactions with this drug and many authors are skeptical of the possible beneficial results. C. Reich and E. Reich (Am. J. M. Sc. 187:71 (Jan.) 1934), because they failed to produce bone-marrow stimulation or increased maturation in rats with the drug, concluded that the "results cast some doubt on the value

of pentnucleotide in the treatment of agranulocytosis" It may be remarked that it is not always possible to carry over *in toto* results obtained from rats to human beings

M. M. Strumia (*Ibid* 187.527 (Apr.) 1934) introduced "**leukocytic cream**," which represents the disintegration products of leukocytes obtained by centrifuging 150 c.c. of whole citrated blood in cream-separating bottles The leukocytic "cream" thus obtained under aseptic precautions is injected intramuscularly daily in divided doses. Whether or not this method has any advantage over that of Reznikoff or Jackson, remains to be seen H Brugsch and J Lautsch (Munchen med. Wchnschr 80 1014 (June 30) 1933) and B. von Bonsdorff (Klin. Wchnschr 13 1079 (July 28) 1934) have used **liver extract** intramuscularly with good results

It is thus seen that the **nucleic acid** derivatives and **liver extract** given parenterally are probably of value, although, because of poor results obtained, some observers doubt this The question of transfusion is a moot one, the reviewer has failed to note any benefit from its use The outlook for recovery appears to vary with the observer In the reviewer's own recent series of cases (unpublished) 9 of 12 recovered Early diagnosis and massive dosage with the above nucleic acid derivatives appear to be of greatest importance

**HEMORRHAGIC DISORDERS. — Classification.** - - Most observers are agreed that, in the main, there are 2 types of hemorrhagic disorders *purpura* and *hemophilia* Various types of purpura, however, are present, differing greatly in the essential mechanisms concerned Some types of purpura are associated with a low blood platelet count (thrombocytopenic) and others with a normal count, the blood-vessel wall being presumably affected (nonthrombocytopenic)

I N Kugelmass (J. A. M. A 102 204 (Jan 20), 287 (Jan 27) 1934), in a comprehensive paper on the hemorrhagic states in childhood, proposes a classification based upon differentiating those cases presenting inherent defects in the blood-clotting mechanism itself from those in which the vascular endothelium is defective He further subdivides the cases as follows

(A) *Cases with defective blood-clotting mechanism*

- 1 Deficient prothrombin in newborn → hemorrhagic disease of the newborn
- 2 Diminished platelets → thrombocytopenic purpura
- 3 Deficiency of fibrinogen as in severe disease of the liver → increased clotting time
- 4 Congenital defects of platelets, etc → hereditary diseases such as hemophilia, thrombasthema, etc

(B) *Cases with defective vascular endothelium*

- Malnutrition, scurvy
- Allergy.
- Chronic infections; chemical poisons
- Hereditary defects of capillary structures

J E Farber (Am. J. M. Sc. 188 815 (Dec) 1934) classifies the hereditary hemorrhagic disorders as follows

- Hemophilia (prolonged clotting time, platelet count normal),
- Thrombopenic purpura (prolonged bleeding time, platelet count low),
- Thrombasthenic purpura (prolonged bleeding time, platelet count normal),

Hereditary telangiectasia (a vascular defect), normal bleeding and clotting time, normal platelet count.

He is unable to put into this group a family of bleeders which he observed in which certain features in common with hemophilia, and certain with purpura were present.

The reviewer is inclined to agree with Kugelmass in dividing the hemorrhagic disorders into 2 main types: (1) those with an inherent defect of one of the blood-clotting factors, and (2) those in which the blood-clotting factors are normal but the vascular endothelium is defective. Clinically, however, 2 types of hemorrhagic manifestations are present: (1) the purpuric, and (2) the type distinguished by poor clotting of blood.

**Etiology.**—Kugelmass (*loc. cit.*) lists the following etiological factors which may be present in a given case showing a hemorrhagic tendency: inadequate dietary (particularly in fats and vitamin C); use of various drugs; irradiation; infections; diseases of the liver; diseases of the spleen; trauma and congestion; and diseases of the bone-marrow. The hereditary factor is of course all-important.

In *hemophilia*, the blood-platelets, although normal in number, are probably unable to form a normal clot; this defect is "genotypic," *i. e.*, carried in the germ plasm. *Purpura* of the *thrombocytopenic form* is present, Dameshek states (New England J. Med., *loc. cit.*) in "destructive" conditions of the marrow (aplasia due to benzol, etc., tumor metastases, leukoses, etc.) and in the "selective" disorder of the marrow known as purpura hemorrhagica (Werlhof's disease) in which the most likely condition is probably that of some defect in the bone-marrow megakaryocytes. It is interesting in this connection to note that J. S. Lawrence and R. E. Knutti (Am. J. M. Sc. 188.37 (July) 1934) found that diminished megakaryocytes were present in only 2 of 6 cases of *purpura hemorrhagica* in which bone-marrow biopsy was done. On this account, these authors felt that there are at least 2 different types of the condition insofar as the bone-marrow is concerned and that the type in which megakaryocytes were present in the marrow would be more likely to profit by splenectomy.

The *nonthrombocytopenic form of purpura* is by far the most common type of hemorrhagic disorder encountered in practice, and in the reviewer's experience is frequently symptomatic of latent infection, a "toxic" process, senility, uremia, rheumatic fever, allergic processes, scurvy, etc.

**Diagnostic Methods.**—Kugelmass (*loc. cit.*) lists the following procedures which are of diagnostic value. (1) A complete blood study (hemoglobin, red and white cell counts, examination of the stained smear). This rules out the presence of leukemic processes and various other hematologic abnormalities. (2) Determination of the clotting time, clot retraction, bleeding time, platelet count to indicate the type of change in the clotting mechanism which involved. (3) In rare cases, when the above factors are normal, the content of fibrinogen, prothrombin, and antithrombin. (4) Application of the tourniquet test (for capillary resistance); occasional use of the microscope for study of the nail bed (of value in hereditary hemorrhagic telangiectasis). K. K. Nygaard (Proc. Staff Meet. Mayo Clin. 9.492 (Aug. 15) 1934) has devised a test of the coagulability of the plasma which he finds is of value in the diagnosis of purpura hemorrhagica. In this condition, the coagulability of the plasma is greatly reduced, despite the fact that the coagulability of the whole blood is normal (test-tube method). Nygaard concludes

that the test-tube method cannot detect finer changes in the coagulability of the blood J. de J. Pemberton (Am. J. Surg. 24:793 (June) 1934) points out the value of study of the morphology of the platelets from a stained smear by a competent hematologist. With this statement, the reviewer heartily agrees; frequently, as much information may be obtained from the single examination of a well-stained smear as from all the diagnostic procedures outlined above.

Because of a low platelet count and hemorrhagic manifestations, the diagnosis of purpura hemorrhagica should not be made immediately, but it should be remembered that the same phenomena are present whenever megakaryocytes are destroyed (as in aplastic anemia, leukemia, etc.). Neither is every case presenting ecchymotic spots an example of purpura hemorrhagica; usually the reverse is true and platelets are abundant. Search should then be made for some underlying condition, infections, etc.

**Treatment.**—For *hemophilia*, no acceptable method of treatment has been found despite the enthusiasm which was engendered by Birch's reports in 1931 and 1932 of the striking therapeutic responses to **ovarian extracts**. R. P. Stetson, C. E. Forkner, W. B. Chew, and M. L. Rich (J. A. M. A. 102:1122 (Apr. 7) 1934), in a carefully conceived study, were able to demonstrate that **theelin** orally, soluble ovarian substance intramuscularly, ovarian substance orally, fresh whole beef ovary orally, aqueous extract of fresh whole beef ovary orally, solid residue of ovarian tissue orally, and theelin subcutaneously all were completely without effect on the coagulation time in 7 cases of hemophilia. Several other authors confirmed these results.

H. W. Jones and L. M. Tocantins (*Ibid.* 103:1671 (Dec. 1) 1934) review the entire field of treatment of hemophilia and conclude that **transfusion of blood** constitutes the best method for the prevention and treatment of acute attacks of bleeding. They also found that intramuscular injection of **whole blood** has seemed to benefit some patients and that **fresh serum** was a satisfactory local hemostatic agent.

In the treatment of *purpura hemorrhagica*, **splenectomy** still holds first place as the method most likely to bring about remission. Pemberton (*loc. cit.*) states the problem from the surgeon's standpoint. He says that the procedure is often life-saving, and that remissions permanent in degree are present in 63 per cent of the cases. The operative hazard in the chronic type is "minimal." He does agree, however, that in cases which are incipient or mild splenectomy is rarely indicated. The reviewer would even go farther. It seems best to attempt all forms of palliative therapy in this disease which is so subject to remissions and relapses. More and more cases of recurrent bleeding are now seen following splenectomy. Among palliative methods to be used, Kugelmass (*loc. cit.*) cites **high protein and high fat diets, elimination of infectious foci, regulation of ovarian dysfunction** by the use of the various pituitary and ovarian hormones, **injection of whole milk intramuscularly, transfusion of blood**, etc. It is also wise, in the reviewer's experience, to use the various **vitamins** in large concentration (A, B, C, D) and possibly to give **liver extract** and **iron**. When bleeding manifestations are numerous, it may be worth while to try some of the newer methods of therapy. the use of **ascorbic acid** (Merck) (vitamin C) given



in solution intravenously, as suggested by A. Boger and H. Schroder (Munchen med. Wchnschr. 81:1335 (Aug. 31) 1934). These authors found that the daily intravenous administration of 100 mgs. ( $1\frac{1}{2}$  grains) of ascorbic acid was effective in controlling capillary bleeding even though the blood platelets might be diminished. The capillary wall is an important factor even when the platelets are reduced. A. Landau and W. Hejman (Presse méd. 42:174 (Jan. 31) 1934) observed that there might be no correlation between the signs of bleeding and the platelet count and bleeding time and suggested that variations in the contractility of the blood-vessels might occur. **Vitamin C** probably acts on the capillary endothelium and this may be the rationale for its action. Similar reasoning is behind the recent use of **moccasin snake venom** therapy in the hemorrhagic states, as suggested by Peck, in 1932 (S. M. Peck and M. A. Goldberger: Am. J. Obst. and Gynec. 25:887 (June) 1933). The venom is used in dilutions of 1:3000 in physiologic saline and injected subcutaneously in gradually increasing doses, usually twice weekly and for a length of time depending upon the type of case concerned. Peck was able to control bleeding in purpura hemorrhagica even though the platelet count did not rise, again suggesting that the venom has a direct action in capillaries.

An antivenom preparation (**antivenin**) has been in use for several years in the control of the hemorrhagic states. K. P. A. Taylor (Am. J. Surg. 21:285 (Aug.) 1933) reports on several cases which have been treated in this fashion (Antivenin may be obtained in 10 c.c. vials and is injected intramuscularly after a preliminary test for sensitivity). Taylor states that the antivenin of certain South American snakes has greater efficacy than that obtained from the moccasin snake. The reviewer, in a limited experience, feels that it is worthy of further trial, in 2 cases bleeding stopped after injection of the antivenin. Whether this was coincidental or not is debatable.

L. Savagnone (Polichinico sez. prat. 41:763 (May 21) 1934) found that **calcium gluconate**, given intravenously, increased the platelet count somewhat, but his results are not at all conclusive. Jones and Rathmell (Tr. A. Am. Physicians 49:277, 1934), in a carefully controlled study, found that large doses of **viosterol** had no real effect on the platelet count, either in normal subjects or those in whom purpura was present.

With respect to **transfusion**, debate still continues regarding the relative merits of the direct *versus* the indirect methods. There can be no doubt, as J. S. Lundy (Minnesota Med. 17:699 (Dec.) 1934) states, that the indirect method with the use of **sodium citrate** is simply and readily performed and no more formidable than any intravenous procedure. Lundy suggests administering the blood slowly—about 15 c.c. per minute. When many transfusions are done, a direct method (the reviewer uses the Scannel) is preferable because the blood is unmodified, there is less handling, etc. From Soviet Russia has recently come an interesting suggestion: the use of **stored blood** obtained either from professional donors or even from cadavers shortly after death. Yu. M. Irger, P. E. Ginzburg, Z. S. Sosonkin, A. S. Mazeleva, P. Yu. Dobruskina and S. N. Verzhynskaya (Novy khir. arkhiv. 32:53 (No. 125) 1934) report on this method and on their studies with experimental conservation of dog's blood. They

conclude that because of various morphologic and biologic alterations which occur, the value of conserved blood for purposes of transfusion is much less than that of fresh blood.

In the nonthrombocytopenic forms of purpura, a vigorous search should be conducted for latent infections, even lues. Calcium in large doses is frequently of value. The reviewer uses **calcium gluconate** 15 Gm. ( $22\frac{1}{2}$  grains) every 3 hours by mouth, together with milk, and at times gives the same drug intramuscularly.

# Diseases of Kidneys

*by*

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**DISEASES OF THE KIDNEY.**—Recent advances in the study of the kidney, its function in health and its behavior in disease, have led to many theories which are contradictory and many classifications which are confusing. From a review of the immense amount of work done in the past year the student emerges armed with much useful data and stimulated by many significant observations. From these, however, he must be prepared to draw his own conclusions, for what often appears to be fundamental knowledge is, in reality, based upon insufficient evidence and the explanation of many important questions still awaits the results of further careful investigation

**ETIOLOGY AND GENERAL CHARACTERISTICS.**—*Bright's Disease.*—A conservative and simple survey of the newer classification, pathogenesis and treatment of nephritis is outlined by W. S. McCann (Pennsylvania M J 37: 199 (Dec ) 1933). He divides Bright's disease into 3 groups:

(A) *Glomerulonephritis*, a generalized disorder of the capillaries, characterized by inflammatory changes in the glomeruli and hematuria.

(B) The *nephroses*, characterized by the degeneration of the tubules and the occurrence of edema from loss of serum albumen. Hypertension and hematuria are absent

(C) The *nephroscleroses*, characterized by ischemic damage to the renal parenchyma due to arterial spasm, arteriolar sclerosis or obliterating arteriolitis. The blood-pressure is usually elevated but hematuria is absent

The associated *edema* may be of 3 types: (a) the hard, nondependent form peculiar to the diffuse glomerulonephritis, (b) the soft, dependent edema with low serum proteins, (c) the soft, dependent edema of heart failure. The therapeutic significance of each type of edema is discussed

McCann stresses the inadvisability of placing all patients with nephritis on a **salt-free, low protein diet**. None of the ordinary foodstuffs of a normal diet, with the possible exception of liver, has been proven injurious to the kidney. An adequate amount of protein is necessary to keep the serum proteins at a normal level and to maintain the general strength and well-being of the patient, which should be the index to treatment. The degree of nitrogen retention in the uremia, he believes, is not directly related to the amount of protein ingested nor does protein restriction for a long period of time prevent the deposit of a great deal of protein when it is again given in the diet. Beneficial results may be secured in many cases of chronic uremia if the general nutritive state is used as the guide to diet rather than the amount of rest-nitrogen in the blood. Uremia, he points out, is a failure of the regulatory functions of the kidney as well as a lack of excretion. This is especially true of uremic acidosis in the prevention of which the patient should be given adequate supplies of base

*Types of Nephritis and Their Management* as outlined by H. A. Christian (J. A. M. A 102: 169 (Jan 20) 1934) may be determined on a basis of (a) time: acute, subacute or chronic, (b) pathology: essential lesion involving the glomeruli or the essential lesion involving the renal vascular system; (c) clinical

effect. urinary changes, edema, increase in blood-pressure or nonprotein nitrogen retention with ultimate uremia.

The concept of a unity of process in nephritis, *i. e.*, that all varieties of kidney lesions are stages of a single process, is less tenable today than that of the duality of lesion in which the dominant renal pathology may be (1) in the glomerulus or (2) in the vascular system. Both types influence the function of the tubules and may result in their degeneration; both types, as time goes on, produce chronic lesions which may be essentially similar in character and effect. Although infection appears to play an etiologic rôle in the glomerular type of nephritis, almost nothing is known as to the pathogenesis of the vascular group. Preventive measures for nephritis are, therefore, very unsatisfactory except for the emphasis to be laid on more thorough treatment of acute infections.

Modern *management* of nephritis recognizes the fact that the disease is not limited to the kidney and must take into consideration the treatment of the patient as a whole. The recommended **diet** is now very liberal and only restricted in the early stages of acute nephritis, when fruit juices and carbohydrates with low fluid intake are indicated. Due consideration must be given to the **removal of infectious foci**. In *acute nephritis* there is practically no indication for drug therapy, with the occasional exception of diuretics, nor is sweating now considered advisable. Cases of *chronic nephritis* must be given an adequate caloric intake and the **diet** should only be restricted when marked nitrogen retention occurs. *Edema* may be controlled by **diuretics** and a high protein **diet** where this is not contraindicated. *Uremia* in its early stages may be handled by a varied **diet** containing adequate protein and vitamin content. **Iron** and **transfusions** are also useful. Severe uremia responds to no treatment, although **bleeding** may be indicated if anemia is not too severe. For the *edema* associated with the cardiac failure of hypertension, therapy must be directed toward strengthening the heart and **digitalis** given continuously. But for the hypertension of chronic nephritis there is no treatment whatever, other than lessening the burden on the cardiovascular system. Luckily, the physician has no ability to lower the high blood-pressure of patients with chronic nephritis, for if renal function is poor, a fall in blood-pressure is one of the worst things that can happen.

**Acute Diffuse Glomerulonephritis** has been studied by F. D. Murphy, J. Grill and G. F. Moxon (Arch. Int. Med. 54: 483 (Oct.) 1934) in a series of 94 cases. They found that nephritis of this type often results from mild forms of infection of the upper respiratory tract, not usually considered as causal factors in acute nephritis. The acute phase of glomerulonephritis may be so mild that it passes unrecognized and no indication of renal damage is observed until the disease has progressed into the chronic stage, when renal insufficiency sets in. There is a period in the course of the disease coming after the early symptoms of the acute phase have subsided that is called the stage of transition, in which the patient is frequently considered cured, but, in reality, the renal lesion continues to be unhealed and progresses toward the chronic stage unrecognized and untreated. The true course of the disease may be followed by the use of the blood urea clearance test and the erythrocyte sedimentation rate, which indicate whether the renal lesion has completely healed or has become temporarily ques-

cent, only to become active later on. Study of cases in the stage of transition is of utmost importance because recognition at this time permits the interruption of the progress of the renal inflammation before chronic glomerulonephritis has come to fruition.

**Nephritis in Infancy**, according to J. B. Rennie (Arch. Dis. Childhood 9. 295 (Oct ) 1934), is a disease characterized by obstinate edema and a reduction of serum protein. In a series of 10 cases in infants less than 18 months of age, 7 cases were fatal, death being due to pneumonia or enteritis in 6 and in 1 to cellulitis. The other 3 patients made complete recoveries, 1 without any special form of treatment. There was no evidence that recovery was due to treatment with high protein diet or ammonium chloride. The edema was ascribed to a fall in the serum protein with reduction in the osmotic pressure. This was a constant observation and the condition differed in this respect from acute nephritis as seen in older children, in which a fall of osmotic pressure below edema level occurred in only 14 per cent. Rennie advises that treatment should be directed toward causing a rise in the serum proteins, as the cure is coincident with their return to normal. He found no evidence that the nephritis resulted from a syphilitic infection.

**Impetigo** appeared to be the cause of acute nephritis in 5 cases reported by L. E. Sutton, Jr. (South. M. J. 27:798 (Sept ) 1934). The etiologic diagnosis was based on the fact that renal manifestations did not occur in any of these cases until the impetigo had been established and the impetiginous symptoms were the only ones complained of at the time of the beginning of the nephritis. Acute nephritis in children is usually attributed to infections. Whether it is due to bacteria which act directly on the kidney or their toxin, carried there by the blood stream, has not been definitely determined. The author's 5 cases, which comprise 28 per cent of the nephritic cases admitted to his clinic during this period, are reported to stress the fact that impetigo, which is frequent in the South, should not be taken lightly, as it is often followed by serious complications.

**Nephritis Following Infectious Diseases.**—That the majority of cases of acute hemorrhagic nephritis are secondary to acute infectious diseases is the conclusion of V. Bie (Ugeskr. f. læger 96:1 (Jan 4) 1934) from an extensive study of nephritis in a Danish fever hospital. Of the various etiological factors, *scarlatina* appeared to be the most important as 5 per cent of the total number of cases were thus complicated. It was also found that only one-half of the cases of nephritis occurred in the third and fourth week of the scarlatina; a fact at variance with the commonly accepted belief. In 9 it developed before this period and in 18 afterward. Fifty-four other cases of nephritis occurred apart from epidemic diseases, and of these, 16 were associated with severe *tonsillitis*, 9 with *erysipelas*, 8 with *pneumonia*, 4 with *septicemia*, 1 with *rheumatic fever* and 1 with *pulmonary tuberculosis*. That hemorrhagic nephritis is a rare complication of these diseases was indicated by the fact that during the same period, 2600 cases of *tonsillitis*, 550 cases of *erysipelas* and 1100 cases of *pneumonia* were treated. Although it is generally believed that nephritis occurs during the third or fourth week from the onset of *tonsillitis* and *erysipelas*, Bie found that in the majority

of cases it appeared at the outset of the primary disease or within a week thereafter.

**Effect of X-ray Irradiation on Kidney Function.**—Among the causes of renal failure attention has been called by F. R. Hagner and S. R. Coleman (J. Urol. 32:27 (July) 1934) to the sometimes fatal effect of x-ray therapy. A case is reported of a patient having a diagnosis of primary carcinoma of the left kidney. The preoperative renal function was relatively good, the blood nonprotein nitrogen being 34.2 mg. per cent and the phenolsulphonphthalein excretion 57 per cent. for 2 hours, of which two-thirds was from the unaffected kidney. In the hope of reducing the size of the tumor and lessening the danger of metastasis, x-ray irradiation was applied in the form of 300 ma. minutes daily for 4 days. The right kidney region was protected and outside the x-ray field. Successful nephrectomy was followed by a period during which the patient appeared to be making good progress, but on the tenth day after operation he developed complete suppression of urine. Appropriate treatment failed to produce more than minimal amounts of urine and, with a steadily decreasing nitrogen retention, the patient developed uremia and died within 2 weeks.

Review of the literature indicated that severe or fatal nephritis has occurred in many cases following application of x-ray therapy to the abdomen, while experimental work on dogs by Daub, Bollinger and Hartman showed that nephritis could be uniformly obtained by irradiation of the kidney with relatively small single applications. The authors therefore emphasize the danger of this form of x-ray therapy and suggest the possibility that lesser degrees of renal damage are often produced which are temporarily masked by the general condition of the patient.

**Rheumatic Infection of the Kidney** occurred as a diffuse glomerulonephritis in 16.2 per cent of 75 cases of rheumatic infection studied by A. G. Palilov (Klin. med. 12:1031 (May 26) 1934). The author considered this alteration a specific manifestation, constituting by its clinical course a distinct cardiorenal type. Among the rheumatic disorders of the kidney, the diffuse vascular alterations in the form of glomerulonephritis predominate over focal infections. The cardiorenal form occurs with greater frequency in patients past 35 years of age, while the cardiac type without renal involvement is more frequent in younger patients. The kidney is affected from the inception of the rheumatic process, involvement occurring in both the benign and malignant types of rheumatism being apparently an identical process in the two. The chronic infection may be progressive in character, terminating in renal insufficiency and uremic coma, with a tendency to exacerbations in the form of acute glomerulonephritis. The mortality rate during the first year was 24.4 per cent for the cardiorenal type as contrasted with 9.5 per cent for the cardiac type. The arterial blood-pressure was higher in the cardiac form, but seldom as high as in nonrheumatic renal disease. The characteristic tendency to hypotonia is likewise manifested in the cardiorenal form of the rheumatic infection.

**Chronic Nephrosis** is believed by E. Matthew and J. D. S. Cameron (Edinburgh M. J. 40:569 (Dec.) 1933) to differ from all other forms of nephritis. A definite diagnosis can be made by means of the Congo red test since Congo



red is eliminated in the urine only in this type of case. The etiology and cause of the various signs and symptoms present in nephrosis are still uncertain. The authors are of the opinion that changes in the kidney itself are primarily responsible for nephrosis and that the site of the significant lesion is the glomeruli and not the tubular epithelium. The permeability of the glomerular membrane is increased so that albumen molecules are able to escape from the blood. Globulin, because of its larger molecules, cannot escape. In the urine, therefore, large quantities of albumen are found but no globulin, while in the blood stream, there is a serious depletion of the plasma albumen, but no change in the globulin content. Since albumen exerts an osmotic tension approximately 6 times that of globulin, there is a great fall in the osmotic pressure of blood which becomes unable to hold its normal amount of fluid. Water, therefore, passes into the tissues in increasing amounts so that progressive edema occurs. It is believed that hypercholesterolemia ensues in an attempt to restore the osmotic pressure. Regarding glomerular permeability as a primary renal change in nephrosis, the authors believe the sequence of events is, therefore, (1) an infective condition, (2) degeneration of the glomerular membrane ending in increased permeability which allows the escape of serum albumen but not of serum globulin or fibrinogen; (3) marked fall in plasma albumen with no fall in plasma globulin; (4) fall in osmotic tension of the plasma; (5) edema which tends to increase; (6) cholesterolemia. They suggest that nephrosis is related to syphilis in many cases, but that syphilitic patients showing albuminuria do not all have typical nephrosis as indicated by their reaction to the Congo red test.

**Lipoid Nephrosis** still bears an uncertain relationship to other forms of nephritis and S. S. Blackman, Jr. (Bull. Johns Hopkins Hosp. 55:1 (Aug.) 1934), in an extensive study of the literature and of 10 classic examples in children, reaches conclusions which differ from certain generally accepted views. Blackman considers that "nephrosis is a particular form of diffuse nephritis in which hematuria, secondary anemia of hemolytic origin and slight elevation of the blood-pressure may occur at times as part of the disease." Acute cases of short duration often occurred without any evidence of "insidious onset." The nonprotein nitrogen of the blood was not constantly elevated. Histologically, the renal lesions consisted chiefly of diffuse changes in the glomerular and tubular epithelium, identical with those which occur in any form of nephritis. Scarred glomeruli were found which were indistinguishable from those of chronic glomerular nephritis, there was no evidence that these were secondary to changes in the tubules, there were no recognizable changes in the glomerular capillaries to account for the albuminuria. The most important histological distinction between nephrosis and nephritis appeared to be the absence in nephritis of coagula-containing fibrin within the glomerular capsules. Under the circumstances, scar tissue formation with destruction of glomeruli and progressive renal insufficiency does not occur. This difference is apparently related to the excretion of fibrinogen in the urine as well as albumen. In the author's 10 cases, characteristic fat deposits were found in tissues other than the kidney and the presence of deposits of neutral fat and cholesterol esters was in no sense specific for lipoid nephrosis. Nephrotic edema could not be explained by mechanical

factors alone and it seemed clear that widespread capillary damage played an important rôle in its production. Blackman believes there is no evidence that lipid nephrosis is a "metabolic" disease, both clinical and experimental evidence pointed to an etiologic relationship between chronic pneumococcal infection and the pathogenesis of some examples of lipid nephrosis. This was supported by the experimental reproduction of lipid nephrosis in animals by means of pneumococcal toxin.

**Nephrosis in Malaria.**—Nephrosis is commonly associated with various diseases of a metabolic or infectious nature. Less frequently seen is its occurrence in the course of a malarial infection. A case of this type which sheds considerable light on the nature of nephrosis is reported by T. B. Menon and D. R. Annamalai (J Trop Med 36:379 (Dec 15) 1933). Malarial parasites were demonstrated in the spleen and malarial pigment in the liver, spleen and other organs. The degenerative changes in the tubules of the kidney with but slight change in the glomeruli supports the view that a necrotizing type of nephrosis is the actual lesion in the kidney, while the marked renal enlargement, the presence of necrosis, and the formation of casts, all show that the change is not a mere fatty degeneration such as is encountered in anemias. The absence of proliferation or crescent formation in the glomerular tufts and Bowman's capsules was quite unlike the appearance encountered in subacute glomerulonephritis. Nephrosis is believed by the authors to be essentially a form of glomerulonephritis in which the injury to the glomerular capillaries is of such a type that no reactive proliferation occurs, but their permeability is affected so that albumin is allowed to escape in large amounts. The presence of malarial pigment in the epithelial cells of the proximal convoluted tubules raises the possibility that this is the hypothetical toxin responsible for the nephrosis. The only possible explanation of its presence in this part of the tubule, in which resorptive functions are not great, is that the pigment was being excreted by the kidney and had caused severe degenerative changes during the process. The malarial infection was apparently of long standing and the patient died in uræmic coma.

**Renal Rickets and Dwarfism.**—Of considerable interest to the pediatrician is the not uncommon association of rickets with chronic nephritis and dwarfism. Three cases of this type have been studied by F. Svensgaard (Hosptalstud 77:977 (Sept 11) 1934) in a boy aged 15 years, one aged 3, and a girl aged 20 months, respectively. In the last two cases the cause of death was uræmia. Necropsy disclosed atrophy of the kidneys and thymus, together with rachitic changes in the bones. The author, summarizing the theories as to the cause of renal rickets, believes that none is adequate to explain all cases.

In an effort to explain the pathogenesis of renal dwarfism, A. Loeschke (Jahrb f Kinderh 143:11 (July) 1934) points out that although the chronic renal disturbance and its sequelæ have undoubtedly a certain significance for the growth of the organism, there are, nevertheless, many factors which speak against their primary importance. He believes, rather, that a congenital component or a defective general constitution is responsible for the gross inhibition of the renal dwarf as well as the renal changes themselves. This assumption is borne out by manifestations of degeneration in the ancestry, familial occurrence

of renal disorders in general and of renal dwarfism in particular, the occurrence of growth disturbances before the onset of the renal symptoms and the occurrence of other malformations in or outside of the urogenital tract. All these factors may be found alone, several together or be entirely absent. In a discussion of the metabolism and pathogenesis of renal rickets, Loeschke states that the phosphatemic curve is higher in renal dwarfism than in children with normal elimination, a fact which corroborates the theory of the stasis of phosphates. The blood sugar curve is also abnormally high and the epinephrine reaction is more pronounced than is the case in normal children. This is attributed to the acidotic condition of children with chronic renal disease. The diastase elimination remains within normal limits. Two factors which probably assume an etiologic rôle are calcium deficiency and chronic acidosis.

The characteristics of renal dwarfism are further discussed by J. W. Ames and M. H. Black (J. Pediat. 3:902 (Dec.) 1933) in their report of a case of renal dwarfism in a girl of 4, whose mother was a morphine addict. The non-protein nitrogen and creatinine of the blood were moderately increased, but a disturbed relation between calcium and phosphorus could not be shown. The most common symptom of rickets, genu valgum, was present, and the deformity has been much exaggerated since the child's improved physical state permits more activity. Other evidence of rickets was lacking, but it is pointed out that the bone changes and the resulting deformities of this disease do not appear until relatively late, the average age of onset, according to Mitchell, being approximately 5 years. Many cases, therefore, develop the syndrome at puberty. Lathrop, in fact, maintains that in well-defined cases x-ray examination may be consistently negative for rickets while other authors consider the skeletal changes quite independent of the general disease.

*Actinomycosis of the Kidney* is relatively uncommon, but the insidious character of its onset, its fatal outcome when untreated, and the fact that recovery depends upon its prompt identification, makes the diagnosis of this condition one of extreme importance. T. S. Kimball and R. B. Hanning (California and West Med. 39:370 (Dec.) 1933) have reported a case in which the lesions were found in the left kidney and right lung. Multiple abscesses were found at necropsy which were not shown in the x-ray pictures taken 2 months earlier, so that the actinomycotic organisms must have reached the lungs in less than that time. The authors believe that the first attack on the kidney took place several months or years before death, but the fatal actinomycotic pyemia arose from an abscess in the kidney. Actinomycosis confined to the kidney may remain practically symptomless even when a large portion of the kidney is involved. In the absence of suggestive history, the diagnosis is made by the pyelographic indications of renal tumor, by the demonstration of actinomyces in the urine, and by the discovery of the fungus in postoperative sinuses. When it can be shown that the infection is confined to one kidney, the *prognosis* is quite hopeful if **nephrectomy** can be performed. Supplementary measures of value are chiefly the administration of **iodides** locally and systemically, the use of **radium** in the wound and of **x-rays** over the area of the wound.

Actinomycosis of the kidney may occur as part of a generalized infection or it may occur without evidence of the fungus in any other organ and without evidence of the port of entry. H. Schneider (Ztschr. f. Urol. 28: 105 (Nov. 2) 1934) reported a case of isolated actinomycosis of the kidney in which necropsy revealed that all other organs were free from actinomycosis and that no port of entry could be found. On the basis of the anatomic picture, it must be assumed that the fungus reached the kidney by way of the blood stream. The author emphasizes the fact that actinomyces may develop in the renal tissues unnoticed for a long time and without perforation into the renal pelvis. Such cases may be very difficult to diagnose, but even if perforation does take place it appears that the renal pelvis, the ureter and the bladder may remain free from actinomycosis. It is apparently possible for the kidney to eliminate the fungus and yet remain free from organic impairment. Actinomycosis seems to favor the development of calculi in the renal calyces. A trauma or a surgical intervention, as in the present case, may lead to a sudden exacerbation of a formerly hidden actinomycosis of the kidney.

**Horseshoe Kidney.**—Horseshoe kidney disease should always be considered in patients presenting an abdominal mass and the triad of characteristic symptoms of umbilical or lumbar pain, gastrointestinal disorders and urinary disturbances. H. Sangree, D. Morgan, T. Klein and R. Trasi (J. Urol. 32: 648 (Dec.) 1934) have found that the symmetrical horseshoe kidney is most commonly constituted by fusion at the lower pole and rarely at the upper pole. Various types of dystopia and inclination to one side or the other may occur, represented by the "caked," the "sigmoid" and the "L-shaped" kidney; these are classed as asymmetrical types. Fused kidneys are more commonly the seat of pathologic changes, especially those incident to urinary stasis, than are normal kidneys. All surgical procedures on horseshoe kidneys should consider the possibility of anomalous vessels often multiple in number and variable in position. The wedge-shaped arrangement of calculi in a urographic examination should suggest the presence of a fused kidney. Concomitant congenital anomalies should always be investigated in a study of a case of horseshoe kidney.

**Renal Calculi** may have a varied pathogenesis among which G. Stuart, W. E. Thompson, and K. S. Krikorian (Brit. J. Urol. 3: 243 (Sept.) 1934) report a case in which *alcaligenes fecalis* occurred in the urine and acted in the capacity of an organic nucleus. The organism was proved on intraperitoneal inoculation to be nonpathogenic to white mice and to guinea-pigs. It was inactive as a urea splitter and failed to support Rovsing's theory of stone formation. Healing of the operative wound was accelerated by autovaccination and the authors believed that the period of convalescence was thus shortened.

**Recurring Pyelonephritis as an Etiological Factor in Nephrolithiasis** was found to have played a predominant rôle in a series of 23 cases treated surgically by H. G. Bugbee (Tr. Am. A. Genito-Urin. Surgeons 25: 121, 1932). The author attaches significance to the fact that there was a frequent change in the urinary reaction from acid to alkaline and that the superimposed coccal infection was followed in all cases by calculus formation. The causal relationship between urinary infections and nephrolithiasis has been often disputed. It is quite

true that renal calculi are often formed in cases free of infection, while many cases of extensive kidney infection show no tendency to stone formation. Nor are the changes in the urine which lead to the precipitation of crystals alone sufficient, since it is well-known that many individuals for long periods of time pass urine containing a sediment of minute crystals of uric acid, calcium oxalate and the various phosphates without showing any tendency to the development of calculi. Bugbee believes, however, from an extensive clinical experience, that infection is probably contributory in a great many cases, in support of which he cites the work of Scholl, who described 10 instances where calculi were formed almost entirely from bacteria. Of Bugbee's cases, only 1 had recurrence and the success of treatment is attributed to the control of the kidney infection through **elimination of foci** in other parts of the body, **increased intestinal activity**, **forced fluids**, **kidney lavage** and **urinary antiseptics**. The author therefore recommends this form of treatment in postoperative cases of nephrolithiasis and stresses the importance of continued treatment and careful follow-up of all cases of kidney infection in the hope of preventing subsequent calculus formation.

**PATHOLOGY.—Renal Glomerulus in Various Forms of Nephrosis.**—Histologic study of the glomeruli in cases of nephrosis reveals the essential importance of the lesions of these structures. In 10 cases of acute simple nephrosis, D. L. Wilbur (Arch. Path. 18:157 (Aug.) 1934) describes the glomerular changes as consisting primarily of irregular thickening of the glomerular basement membrane and less often of an increase in number and swelling of the endothelial and epithelial cells of the tufts. In the majority of cases these changes were considered independent lesions, the result of associated hypertension, arteriosclerosis or other complicating renal disease. They did not resemble the lesions seen in cases of clinical glomerulonephritis. In 31 cases of acute simple nephrosis the glomeruli showed, as a rule, normal tufts with occasional minor variations consisting of variable amounts of debris in the capsular spaces, swelling, degeneration, a slight increase in the number of endothelial or epithelial cells, and occasionally slight irregular thickening of the glomerular basement membrane. These changes appeared to be degenerative and quite unlike those observed in cases of glomerular nephritis or lipid nephrosis. Of 13 cases of bile nephrosis, the majority occurred in persons in whom the glomeruli appeared histologically normal, although a moderate amount of granular material was also noted in the capsular spaces. In 3 cases of chemical nephrosis, the glomeruli appeared normal except for congestion, desquamation of many of the epithelial cells and granular material in the capsular spaces. In 2 cases of eclampsia, the glomerular changes were similar to those described by Bell, while in 1 case of hyperemesis gravidarum, the glomeruli appeared normal. The renal lesions in eclampsia are concluded to be secondary and, although distinct and probably degenerative, their precise nature cannot be stated at present.

**Histological Changes in the Kidney in Malignant Hypertension** were described by E. F. Cam (Arch. Int. Med. 53:832 (June) 1934) as being diffuse and involving the glomeruli, tubules, arterioles, arteries and interstitial tissues. The most prominent changes appeared in the arterioles. They consisted of extreme narrowing of the lumen, apparent increase in the number of endothelial

cells; subendothelial, fatty and hyaline degeneration, apparent thickening of the tunica media, and an increased amount of connective tissue, chiefly in the tunica adventitia. The ratios of the wall to the lumen of the renal arterioles were remarkably reduced. The kidneys were not markedly or uniformly decreased in size.

**Renal Lesions of Rheumatic Fever** in a series of 16 cases were studied by J. L. Blaisdell (Am. J. Path. 10:287 (Mar.) 1934). A perivascular inflammatory reaction of the acute nonsuppurative type affecting the smaller arteries and arterioles was present in 8 cases, evidence of perivascular scarring was noted in 4, while a recurrent type of inflammation was encountered in 2 patients. The inflammatory reaction was usually found in the adventitial or periadventitial tissues, with occasional infiltration and destructive changes in the medial coat. Intimal changes, consisting of an endothelial swelling and proliferation, were inconstant. Glomerular damage, which was well marked in only 1 case, is regarded as dependant chiefly on nutritional disturbances, brought about by vascular changes. Little evidence of active or healed inflammatory processes was noticed in the glomeruli. The lesions described bear a close resemblance to perivascular foci of inflammation found in the myocardium and may be looked upon as constituting a definite type of interstitial nephritis. Blaisdell believes, however, that alteration in structure is seldom sufficient to justify a diagnosis of renal disease during life.

**The Disappearance of Glomeruli in Chronic Kidney Disease.** In chronic renal disease in man and in experimentally-produced glomerular injury in rabbits, a large proportion of the glomeruli in a given kidney may disappear, leaving no recognizable trace. A. R. Moritz and J. M. Hayman, Jr., (Am. J. Path. 10:505 (July) 1934) found that in the case of rabbits there was not even any condensation of the interstitial connective tissue to indicate the loss of parenchyma, while in man, although interstitial fibrosis was a constant observation, recognizable glomerular scars were not numerous enough to account for more than a fraction of the obliterated glomeruli. The authors point out that if so large a proportion of the glomeruli in chronic renal disease can disappear without a trace, the final histologic examination of the kidney may give less information concerning the pathogenesis and severity of the disease than is commonly thought. If a kidney having a normally expected number of 1,000,000 glomeruli can lose as many as three-fourths of these without leaving recognizable scars, it is not fair to assume that the changes affecting the remaining one-fourth were necessarily the same as those that occurred in the glomeruli that had disappeared. The final pathologic diagnosis of the kidney is frequently made on a basis of the preponderant change seen and this may involve a weighing of the evidence of arteriosclerosis against the evidence of inflammation. If complete glomerular disappearance occurs to the extent indicated in this investigation, the final pathologic picture may throw but little light on the pathogenesis of certain types of chronic renal disease.

**Retinal Lesions in Chronic Glomerulonephritis.**—Thirty-two cases of chronic glomerulonephritis were followed by E. W. Cannady and J. P. O'Hare (J. A. M. A. 103:6 (July 7) 1934) over a period varying from 6 months

to 14 years. Considering the retinal lesions in these cases, it was found that in 30, retinal changes developed before death, while 25 showed the picture of an advanced state of arteriosclerotic retinopathy or hypertensive neuroretinopathy. It was found impossible in most cases to make an ophthalmoscopic differentiation between the lesions of chronic glomerulonephritis and primary vascular hypertension. Hypertension was the most common etiologic factor in the retinal arteriolar lesions, but these changes usually preceded the development of the more advanced retinopathies. The appearance of arteriosclerotic retinopathy or hypertensive neuroretinopathy was found to indicate a very poor prognosis. The maximum duration of life after the appearance of these lesions was 23 months, but the average for the entire series was less than 7 months.

It is of interest in connection with nephritic retinitis that H. Ehlers (Hospitalltid 76:1029 (Oct.) 1933) believes this condition may be influenced by diet. He noted the fact, which he considers significant, that during the years of rationing in Europe from 1918 to 1921, the number of cases of nephritic retinitis was definitely reduced. He believes, however, that the frequency of this disorder is increasing and from a study of 56 cases he was unable to find any evidence of notable improvement in prognosis

**PATHOGENESIS AND FUNCTION.—*Relation Between Renal Histology and Clinical Picture of Nephritis.***—In reviewing the subject of kidney disease, J Gray (Brit M J. 2:1165 (Dec 23) 1933) points out that a correlation between symptoms and pathological changes is difficult, since the physiology of the kidney is not yet completely understood. He accepts, however, the filtration reabsorption theory of Cushney, and believes that although all parts of the kidney are affected in nephritis, the glomerular changes are in all cases the most important. In acute nephritis there is both a diminished amount of blood passing through the glomeruli and an increased permeability of the capillary membrane. The former accounts for oliguria and nitrogen retention; the latter, for albuminuria and hematuria. Edema is probably due in part, at least, to generalized capillary damage, although this has never been demonstrated histologically. The hypertension of nephritis is the more remarkable for its inconstancy and its cause at the present time is entirely unknown. Chronic nephritis exhibits destruction of many glomeruli, those which survive being relatively normal in function, other than that, their compensatory overactivity causes polyuria from inadequate reabsorption in the tubules. In cases where inflammatory changes in the glomeruli have caused increased permeability, there may be albuminuria, loss of serum protein and edema. Parenchymatous nephritis or nephrosis has a varied histology, but is primarily characterized by increased capillary permeability, with albuminuria and edema, permeable glomeruli are always present in sufficiently large numbers to explain the prolonged absence of renal insufficiency, hypertension and uremia. The author points out that tubular damage is only likely to produce failure to concentrate the urinary filtrate to a normal degree and this results in uremia only when the tubular necrosis is so extensive that it permits mechanical and unselected reabsorption into the blood stream.

To explain renal insufficiency in nephritis, H. Kutschera-Aichbergen (Ztschr. f. klin. Med 127 57 (May 24) 1934) distinguishes 2 forms of nephritis *i. e.*, the intrainfectious and the postinfectious. The first form is attributed to a direct bacterial impairment of the renal tissues, while circulatory disturbances predominate in the second form. In *intrainfectious* nephritis, serious renal insufficiency never occurs during the acute stage and only occurs during the chronic stage, when most of the glomeruli are closed by finely granular emboli. In *postinfectious* nephritis (hypertensive nephritis) insufficiency may develop during the acute as well as the chronic stage. The characteristic sign of hypertensive nephritis is the reduction of water elimination. This disturbance is not so much the result of inflammation as of an insufficient blood perfusion of the glomeruli. In chronic hypertensive nephritis 2 different forms of renal insufficiency should be differentiated: (1) cases in which there are severe morphologic changes, and (2) cases in which the lesions of the renal parenchyma are relatively slight. In the latter group, a functional factor is responsible, especially a disturbance of the renal circulation. A comparison of the different manifestations of insufficiency with the morphologic changes in the various renal elements permits the following conclusions about the physiology of the human kidney which, in the author's opinion, corroborate and supplement Volhard's theory: (1) Water elimination takes place primarily through the glomeruli. If the glomeruli do not function, their activity may be taken over, although insufficiently, by the main portion of the uriniferous tubules. (2) The concentration of urine is due to the secretory function of the epithelium of the main portions of the tubules. In addition to this, a reabsorption of water by Henle's loops must be considered.

**Relationship of Blood-pressure to Kidney Function** Glomerular filtration depends upon the maintenance of an adequate perfusion pressure in the renal arteries. Of great clinical importance is the extent to which renal function is altered by changes in blood-pressure. This applies not only to the variations in the normal arterial pressure, but also to the effect of hypertension associated with nephritis and whether or not this is a compensatory mechanism, interference with which may be deleterious to the patient. In the experimental animal, G. Medes and C. J. Bellis (Am. J. Physiol. 107 227 (Jan. 1) 1934) have succeeded in demonstrating the effect on glomerular filtration of altering the blood-pressure in the renal artery. Large dogs were used, the renal and carotid arterial pressures recorded and the creatinine clearance estimated repeatedly at 15-minute intervals. It was found that when the abdominal aorta was obstructed, the systemic pressure remained practically unchanged, but a marked fall occurred in the renal blood-pressure. This was accompanied by a corresponding decrease in creatinine clearance. A fall of renal pressure from 135 to 80 mm Hg. caused a decrease in the creatinine clearance from 27 to 6 c.c. per minute. Kidney function, therefore, depends not only on renal blood flow, but is proportional to the local perfusion pressure as well. According to the authors, these results substantiate the theory of Rehberg that the blood creatinine clearance is accomplished by filtration rather than by tubular secretion.

A similar demonstration of the relationship of glomerular filtration to blood-pressure was made in man by H. C. A. Lassen and E. Husfeldt (J. Clin. Invest-



igation 13:263 (Mar.) 1934) Taking advantage of the fact that under spinal anesthesia the blood-pressure undergoes a marked fall, they estimated the creatinine clearance in 4 cardiorenally-healthy young men while they were under spinal anesthesia. They observed that (1) during the rather considerable fall of blood-pressure which appeared when the effect of the anesthesia was at its height, the glomerular filtration decreased markedly and to a degree which corresponded fairly well with the fall of blood-pressure. (2) At the same time the concentration index increased significantly and remained high, or rose even further during the subsequent gradual rise of blood-pressure. Thus, the tubular function was normal or even hypernormal, as far as the reabsorption of water was concerned, at the same time that the effect of the spinal anesthesia was at its height and glomerular filtration was lowered. (3) During the fall of blood-pressure there was an enormous decrease in the volume of urine, partly on account of considerable reabsorption of water in the tubules, partly because of the lowered filtration in the glomeruli. In 3 control experiments, the course of the glomerular filtration was followed under spinal anesthesia during which the fall of the blood-pressure was counteracted by injections of ephetonin. Ephetonin was able to maintain at the same time both a normal blood-pressure and a normal glomerular function, while the function of the tubules remained unaffected. The relation found between the blood-pressure and the kidney function can be readily explained in accordance with the filtration reabsorption theory.

There remains the problem of whether a similar decrease of glomerular filtration occurs on lowering an arterial pressure which is persistently elevated. In 1856, Traube postulated that hypertension in cases of nephritis is a compensatory mechanism to overcome an abnormal resistance to blood flow in the kidney and to maintain the efficiency of the renal excretory function. This explanation, although widely accepted, has never been conclusively demonstrated, but some support is lent to it by the evidence cited above, *vide*, that kidney function is markedly diminished by a decrease in renal blood flow or blood-pressure below the normal value. I. H. Page (J. Clin. Investigation 13:909 (Nov.) 1934) has, therefore, investigated the question in a study of 6 patients, 2 with malignant hypertension, 2 with moderate hypertension, and 2 with Bright's disease. Blood-pressure and urea clearance tests were repeated periodically over an interval of 3 months to a year, during which time the blood-pressure was significantly lowered. In 2 cases this occurred spontaneously, in the others it was effected by means of sodium thiocyanate, aqueous colloidal sulphur or unilateral renal denervation. Despite the marked changes in blood-pressure, Page could demonstrate no alteration of the urea clearance. He concluded, therefore, that the efficiency of the kidneys is unaltered by a fall of arterial pressure, that hypertension does not appear to assist in the maintenance of renal efficiency, and that hypertension is unlikely to be a compensatory mechanism in patients suffering from chronic nephritis.

**Edema.**—The mechanism of nephritic edema has been investigated by J. S. Dunn, E. G. Oastler, and S. L. Thompsett (J. Path. and Bact. 38:421 (May) 1934), who produced nephritis in experimental animals by means of corrosive mercuric chloride, potassium bichromate and uranium acetate. Extensive sub-

cutaneous edema and serous transudates occurred when the renal lesions were sufficiently severe and the animals ingested a sufficient amount of fluid. The greater amount of edema in uranium nephritis appeared to be due to severe damage to the renal structure combined with a low general toxicity and non-interference with nutrition. The essential cause of edema in experimental tubular nephritis, they conclude, is failure of the kidney to excrete sufficient fluid, oliguria, they attribute to failure of the damaged renal tubules as conducting channels.

According to Starling, there are 2 principal antithetic factors which determine the occurrence of edema, *i e*, the *capillary hydrostatic pressure*, which favors the transudation of fluid from the vascular system, and the *colloud osmotic pressure* of the blood, which favors the retention of fluid in the vascular system. These factors are modified by the ratio of serum albumin to serum globulin, the elasticity of the tissues, the constant variations in the hydrostatic pressure, the degree of permeability of the capillaries, and the quantitative relationship between electrolytes in the blood and tissues. Salt, if given alone, is rapidly excreted, if given with water it causes slight fluid retention, and if given in the presence of a lowered serum osmotic pressure in nephritis, it causes marked edema. J. B. Rennie (*Quart J Med* 2: 521 (Oct.) 1933), in a clinical study of the relationship of serum proteins to edema, points out that the kidney itself is not directly responsible for edema, but only for the occurrence of conditions which permit the formation of edema. Thus, in nutritional edema there is no kidney lesion, but he was able to demonstrate in all cases a consistent lowering of the serum proteins. Similarly, in cardiac edema a reduction of the serum albumin was present but, in addition, there was an increase in the venous pressure. The fall in serum osmotic pressure was a constant finding in the nephrotic syndrome but the development of edema was sometimes prevented by a salt-free diet. Rennie found evidence that in acute nephritis the rise in blood pressure also plays a rôle in the production of edema, it, furthermore, appeared possible that the low serum protein was not due alone to proteinuria or to insufficient protein intake, but rather to a *defective protein synthesis*. No way is known at present of remedying defective protein synthesis, but he recommends a drastic reduction of salt in the diet as a palliative measure. A **salt-free diet** is indicated at any stage of nephritis, but when salt is thus restricted, there may be no objection to unrestricted fluid intake.

Other factors, however, may be necessary to explain the edema which occurred in a case of mercuric chloride poisoning reported by F. Roth and N. Szent-Gyorgyi (*Klin Wchnschr* 13: 726 (May 19) 1934). The authors called attention to the fact that edema in this type of nephritis is generally attributed to a lowering of the serum osmotic pressure proportional to the loss of serum protein from albuminuria. Their case, however, presented a serum osmotic pressure which remained normal until death. In the absence of other adequate interpretation, they point to the possible significance of an alteration in the fibrinogen content of the blood which occurs also when mercurial therapy is administered in the form of novasurol. It is incidentally stated that in their hands

the protein content of the blood was most conveniently estimated by the simple determination of the serum osmotic pressure.

W. T. Longcope (New England J. Med. 210:1243 (June 14) 1934), emphasizing the plasma protein content among the causes of edema, discusses its relationship to nutritional disturbances. Since albumin forms about 60 per cent of the plasma protein and has an osmotic pressure of 5.5 mm. Hg. per gram, while the globulin content of the plasma is only 40 per cent. with an osmotic pressure of 1.4 mm. Hg. per gram, it is chiefly a continuous loss of albumin which predisposes to the formation of dropsy. The most common and important method of depriving the body of protein is through the long or excessive reduction of protein in the diet, and the edema of undernutrition, which has been recognized for centuries as "prison dropsy" and "hunger swelling" and which was common in the central European countries during the World War. Edema due to low plasma protein is common in many different types of disease, including diabetes mellitus, neoplasms, infections of various sorts, anemia and diseases of the liver. It has been shown that assuming the erect posture in the presence of a low plasma osmotic pressure may precipitate a latent edema by increasing the hydrostatic pressure similarly to cardiac failure. The factor of heart failure must also be considered in cases of anemia, since its effect may exaggerate that of the low serum protein content usually associated with anemia. Fibrinogen is elaborated by the liver and if the same is true of other serum proteins, it is possible that many cases of edema are due to defective protein synthesis associated with disturbances of hepatic function. There is very suggestive evidence of this from the reduction of plasma proteins repeatedly observed in cases of hepatic cirrhosis and acute yellow atrophy of the liver.

**Allergy in Relation to Urogenital Tract.**—There is much clinical evidence as well as experimental data to support the conception that nephritis in many instances may be an allergic manifestation. It remains unknown, however, whether an allergic reaction can be the primary cause of nephritis and even as a contributory factor its rôle is not clearly understood. D. M. Davis (Southwestern Med. 18:5 (Jan.) 1934), in a review of the relationship of allergy to the urogenital tract, has called attention to the suggestive experimental evidence obtained in animals. Thus, perfusion with tuberculin of the kidney of a tuberculous guinea-pig may produce extensive necrosis within 4 days. The same lesions are found in sensitized rabbits after injection of protein. Clinically, it has been shown that paroxysmal hemoglobinuria may be an expression of allergy to cold and that in severe attacks of anaphylaxis, albumin, casts and blood may appear in the urine. Up to the present time, however, permanent renal damage has not been convincingly demonstrated, although many cases of chronic nephritis are strongly suspected of having an allergic background. Davis emphasizes the need of more thorough investigations in this question in which the observations thus far are so suggestive but still await proof.

**Nephritis Due to Exposure to Cold.**—This question has been clarified by A. J. Nedzel (J. Urol. 31:685 (May) 1934) who demonstrated that the normal kidney responds to the exposure of the skin to cold and heat in the same manner as the skin itself. He observed that the application of ice-bags to the skin pro-

duced a fall of temperature on the surface of the kidney more quickly than in the blood of the abdominal aorta, while superficial application of heat raised the renal temperature above that of the blood in the abdominal aorta. In the denervated kidney, the temperature appears to follow closely that of the blood stream. The differences in the rise and fall of temperature in the normal kidney are therefore ascribed to a vasomotor reflex from the skin, producing renal vasoconstriction and dilatation. These vasomotor reactions are accompanied by increased permeability of the capillary blood-vessels and through them pathogenic bacteria in the blood are permitted to invade the kidney. Streptococci present in the upper respiratory tract after exposure of a person to cold may be absorbed into the circulation and during the same exposure the kidneys, which are suffering from reflex circulatory disturbances from the skin, present favorable conditions for localization of wandering microorganisms in the blood. The settlement of these latter produces inflammation of the kidney, or nephritis. Many infections of the upper respiratory tract are not accompanied by infection of the kidneys, although the urine often shows the presence of various microorganisms apparently excreted by the kidneys without harm. This fact indicates that the presence of virulent bacteria in the blood is not alone adequate to produce nephritis without sufficient change in the walls of the renal blood-vessels for the bacteria to permeate them.

**Uric Acid in Pathological Renal Function.**—In a series of cases of scarlet fever, W. Voigt and H. Schulke (Klin. Wchnschr. 13: 973 (July 7) 1934) made daily estimations of the blood uric acid content throughout the course of the disease. They found that during convalescence there occurred in all cases a period during which the blood uric acid became elevated. This increase of from 1 to 2 mg. per cent appeared between the twelfth and twenty-fourth day of the disease, *i. e.*, at precisely the same time as the manifestations of obvious nephritis in other scarlet fever patients in whom this complication occurred. In cases where a cantharides blister had been produced, a simultaneous increase in uric acid was found, both in the blood and in the inflammatory fluid. The authors were unable to explain this phenomenon on a basis either of a secondary infection, such as lymphadenitis, or by an involvement of the liver, since the latter usually leads to depression of the blood uric acid. They attribute it, therefore, to a renal disturbance, an interpretation which is substantiated by the coincident time relationship to scarlet fever nephritis and the quantitative similarity of the rise in both conditions. From these observations it was concluded that during every convalescence from scarlet fever there is a definite disturbance of kidney function. Voigt and Schulke believe that this disturbance is an allergic manifestation.

**Permeability of Kidney to Bacteria.**—Can bacteria circulating in the blood stream be excreted by the normal kidney? If so, to what extent may they be the cause of nephritis and other infections of the urinary tract? Is the renal excretion of bacteria a physiological method for their removal from the blood stream? Previous experimental work on the subject has given ambiguous results and a further attempt at answering these questions has been made by H. J. R. Kirkpatrick (Brit. J. Urol. 6:1 (Mar.) 1934). In a large series of rabbits, suspensions of various types of virulent bacteria were injected directly

into the blood stream. The urine, previously sterile, was thereafter collected under aseptic conditions and cultured for the organism and examined for evidence of renal damage. The kidneys were also examined to determine whether bacteria had penetrated the renal tissue and whether inflammatory changes had resulted. It was found that under normal physiological conditions bacteria were neither excreted in the urine nor did they escape from the renal capillaries into the tissues. When diuresis was caused simultaneously with the injection of large numbers of bacteria, a few organisms escaped into the urine and a few could be found singly and in pairs within the renal capillaries. Only when a toxic action of the injection itself was obvious was there any evidence of damage to the kidney. Kirkpatrick concluded that bacteria may pass from the blood into the urine in the absence of detectable renal damage, but that permeation of the normal kidney is not a mechanism in the production of bacteriuria under natural conditions. These results are very interesting, since they indicate that a blood stream infection may not necessarily involve the kidney. They afford very suggestive evidence that the pathogenesis of acute nephritis involves factors other than bacterial infection alone and, as discussed elsewhere, an allergic reaction is probably contributory. Evidently it is only glomeruli which are already abnormal which become the site of diffuse infectious inflammation.

***Pyelovenous Reflex and Intrarenal Absorption.***—It is well known that bacteria infecting the lower urogenital tract are under certain circumstances capable of ascending to the kidneys, which may thus become involved in the infectious process. This phenomenon was studied by E. Ciocca (*Arch. ital. di chir.* 36: 645 (May) 1934), the experiments being performed on dogs and rabbits. It was found that microorganisms, when introduced in suspension into the ureters, may pass through the kidney and be recovered from the blood stream of the efferent renal vein within 10 minutes' time and usually at a pressure of scarcely 10 mm. Hg. With opaque substances, x-ray images could be obtained in the kidneys which were attributed to a pyelocanicular reflex. The author explained his results as being a manifestation of intrarenal absorption through the epithelium of the tubules, a phenomenon which appears to account for the occurrence of certain renal infections such as cortical abscesses and infectious nephritides.

***Plasma Magnesium and Magnesium Excretion.***—Although Epsom salt has been used as a cathartic since 1675, little has been known regarding the amount of magnesium actually absorbed from the bowel and excreted from the kidneys and the effect of renal insufficiency on this process has been entirely overlooked. A. D. Hirschfelder and V. G. Haury (*J. Biol. Chem.* 104: 647 (Mar.) 1934) in a study of the subject, found that the average plasma magnesium content of 7 normal men was 1.85 mg. per cent, that on the injection of magnesium it rose to an average of 2.09 mg. per cent, and that an average of 42 per cent of the injected magnesium was excreted in 24 hours. The percentage of magnesium was fairly constant, being independent of both the dose and the plasma content. In normal men and animals, ordinary doses of Epsom salt scarcely altered the plasma magnesium. In nephrectomized animals or animals with injured kidneys, however, the injection of magnesium sulphate caused a rapid and intense increase

in plasma magnesium which often produced coma Hirschfelder and Haury believe from these results that many cases of coma in nephritic individuals, supposed to be uremic coma, are produced by the use of magnesium salts as purgatives, and adds that resuscitation could probably be effected by the intravenous injection of calcium salts Magnesium sulphate is, therefore, contraindicated in patients with renal insufficiency and sodium sulphate should be the saline of choice Magnesium excretion appears to be depressed more by injury of the tubules than by injury of the glomeruli.

**Effect of Barbiturates in Experimental Nephrosis.**—The choice of sedatives to be used in cases of nephrosis has been shown by W S Murphy and T Koppanyi (J. Pharmacol and Exper. Therap 52 7 (Sept ) 1934) to be a matter of considerable importance. In a series of dogs and rabbits, experimental nephrosis was produced by the administration of tartaric acid, potassium chromate or uranium acetate until severe renal damage was indicated by deficient phenol red excretion and the presence of marked albuminuria The effect of sodium barbital was then observed, as well as that of some of the more briefly acting barbiturates, including nembutal, pernocton, neonal, pentobarbital and sandoptal Nephrotic animals exhibited a decreased elimination of barbital with a low concentration of the drug in the urine and increased retention in the blood and tissues When *sodium barbital* was administered in anesthetic doses, the animals failed to recover and died in uremic coma Recovery occurred, however, in all instances where those barbiturates were administered which are partly broken down in the blood stream and do not depend entirely upon renal excretion It is evident from these observations that giving sodium barbital in cases of renal insufficiency is not without an attendant danger, since it may be retained in the body in sufficient concentration to precipitate coma The comparative safety of the other barbiturates is apparently related to their greater independence of renal function for elimination

**Deficiency in Sodium Chloride Content of Blood.**—This condition is discussed by E Kohlschutter (Deutsche med Wchnschr 60 8,7 ( June 1 ) 1934) as the cause of a special form of *uremia* in which there may be no distinct anatomic changes in the kidney Uremia of this type may follow the loss of excessive amounts of fluid from hyperemesis or persistent diarrhea The increased nitrogen retention and other uremic manifestations arise, not from a primary renal insufficiency, as might appear from the clinical impression, but rather from the loss of chlorides This condition should be expected whenever there is a history of dehydration preceding the uremic symptoms It is important, therefore, to determine the blood chloride content whenever a high rest-nitrogen appears under these circumstances, as the correct diagnosis may be confirmed and the danger of a low chloride uremia may be averted by the administration of saline The author's further investigations of the subject indicate that there is no danger of this type of uremia following the use of diuretics such as salyrgan, which often lead to a considerable loss of water and sodium chloride with moderate nitrogen retention.

**Low Concentration of Urea in the Blood.**—This subject was studied by A. E Osterberg and N. M. Keith (J. Lab and Clin Med 20. 141 (Nov ) 1934)

from the records of 25 patients in which the blood urea values were less than 10 mg per cent. Among these cases a wide variety of disorders was manifested and several suffered from serious chronic disease, including pulmonary tuberculosis, encephalitis, diffuse lesions, chronic suppuration, diabetes mellitus, duodenal ulcer and Addison's disease. In some cases, chronic renal lesions were present, such as bilateral pyelonephritis, bilateral hydronephrosis, tuberculosis of the kidneys, and the diffuse nephritis associated with lupus erythematosus. In the majority of cases the occurrence of a low blood urea content appeared to be associated with a disturbance of water balance. Excessive polyuria with a correspondingly increased fluid intake seemed the most plausible explanation in *diabetes mellitus* and *diabetes insipidus*. Similarly, in *duodenal ulcer with obstruction*, the water metabolism may be greatly upset, since such cases receive large intravenous injections of fluid, it may have been upon this factor that the low urea depended. However, in other cases no definite organic lesions or marked physiologic disturbances could be demonstrated and the symptoms were described as being due to nervous exhaustion. Difficult to understand were the cases in which a low blood urea accompanied bilateral renal disease. In one such case associated with *lupus erythematosus*, the patient was ingesting and excreting large quantities of water and was on an inadequate diet. The blood urea fell to 6 mg. per cent. Apparently during a temporary process of healing in the kidneys, water and urea were readily excreted while the production of urea was decreased. Another case which developed a blood urea of 6 mg per cent was one of *chronic pulmonary tuberculosis* in which albuminuria and cylindruria appeared during the terminal stages. At necropsy there were no histological abnormalities demonstrable in the kidneys. Thus, it is possible to have a very low value for urea in patients with abnormal kidneys whether the renal disturbance is due to demonstrable histologic changes or to physiologic abnormalities.

**Effect of Liver in Nephritis.**—The question of the effect of ingested protein on the damaged kidney is still largely unsettled. The present tendency, as elsewhere discussed, is not to restrict protein to the extent previously thought necessary. In cases with marked albuminuria or low serum protein it is clearly advisable to counteract the deficiency with a high protein diet but even in chronic Bright's disease, Kreutmann and McCann, contrary to former opinions, have noted a general improvement after the ingestion of large amounts of protein. While the theoretical contraindication lies in the inability of the damaged kidney to excrete nitrogenous products, the fact of the matter has never been quantitatively determined. Further light has been thrown upon the question by the work of A. Chanutin (Arch Int Med 54:720 (Nov.) 1934) from his study of the effect of diets containing varying amounts of liver in experimental renal insufficiency in rats.

The feeding of diets rich in liver to white rats has consistently produced renal damage and it has been concluded that liver is the most nephrotoxic of the natural foodstuffs studied. Chanutin found that in intact and unilaterally nephrectomized rats, the ingestion of liver was followed by enlargement of the kidneys, which was roughly proportioned to the nitrogen content of the diet. The azotemia was more marked in those animals receiving the diets containing more liver but the

renal function appeared to be unaffected. An appreciable number of unilaterally nephrectomized rats had slightly increased blood-pressures. In the partially nephrectomized rats, whole liver caused the excretion of increased quantities of dilute urine and had a definite effect on the early appearance of hypertension. The diet containing liver residue or liver extract had no effect on the volume or specific gravity of the urine and was seldom followed by hypertension despite evidence of renal damage. The degree of azotemia appeared to depend on the amount of nitrogen in the diet but, as in human beings with damaged kidneys, there was no exact relationship between the retention of nitrogen and the morbid symptoms.

In commenting on his results Chanutin pointed out that the low protein diet delayed but did not prevent the appearance of hypertension and, in addition, there was little retention of nitrogen, albuminuria and polyuria. On the other hand, the high protein diet showed no marked effect on blood-pressure, albuminuria or renal changes despite the increased excretion of dilute urine and the marked nitrogen retention. In other words, there is justification for the clinical use of a low protein diet in nephritis, since the nitrogen retention is thereby less marked, but otherwise it has still no proven effect in amelioration of other nephritic symptoms.

**DIAGNOSIS AND RENAL FUNCTION TESTS.**—The modern diagnosis of renal pathology and the estimation of renal function has come to depend for its completeness not only upon the observance of edema, hypertension and the more conspicuous urinary changes, but also upon the determination of the precise manner in which the kidney mechanism has been affected by disease and the effect which this has produced upon the body as a whole. Inability of the kidney to excrete one substance or to retain another leads to the development of varying syndromes due to altered relationships in the constituents of the blood. The more accurately these altered relationships are identified, the more logically can therapy be applied, for in Bright's disease it is the entire body which must be treated and not the kidneys alone. This necessity for greater precision in the appraisal of renal function has led to the development of many so-called function tests and to considerable confusion in the minds of most physicians as to their application, limitations and significance. It should, therefore, be pointed out that in the average case of nephritis it is seldom necessary for practical purposes to utilize more than a few of the simpler diagnostic methods. Such economy is justified, however, only by a thorough understanding on the part of the physician of just what part of the kidney function is exhibited by the test, how far the values obtained are influenced by extra renal factors, to what extent the result of the test may be expected to coincide with that of other tests, and what functions of the kidney are left unexplored. All this presupposes a knowledge both of the modern conceptions of renal physiology and of the general physiology of the body with which it is interdependent; also, a familiarity with the comparative results expected and obtained in various conditions at the hands of reliable observers. A few of the more recent diagnostic methods will therefore be summarized.



**Significance of Concentration and Dilution Tests in Bright's Disease.**

—The urea clearance test measures the ability of the kidney to excrete urea; the various concentration tests are chiefly adopted to a measurement of the ability of the kidney to excrete mineral salts. An interesting study of the comparative value and application of the concentration tests with the urea clearance has been made by A. S. Alving and D. D. van Slyke (J. Clin. Investigation 13:969 (Nov.) 1934). They found that the concentration tests done after adequate preliminary régime and with correction for the effect of protein on the specific gravity were sufficiently sensitive for the *qualitative* determination of damaged renal function. The Mosenthal test, in which the maximum urine specific gravity is noted during the spontaneous variations of the day without preliminary régime, yielded similar, although perhaps less sensitive, results. For estimating the *extent* of renal damage, however, the concentration tests did not appear to be suited, as the disagreement with the urea clearance test was often extreme. Thus, a patient who has practically recovered from acute nephritis and regained a normal urea clearance may, by concentration tests, continue for some time to yield urine of 1.009 to 1.012 specific gravity, the same as a patient in terminal uremia with 3 to 5 per cent. of normal urea clearance. In chronic cases sufficiently advanced to show urea clearances 20 to 30 per cent. of normal, concentration tests may already show minimal specific gravities and will then reveal no further changes during the subsequent progress of the disease, while the urea clearance continues to fall until it reaches the uremic level of 3 to 5 per cent. The extent of the urine specific gravity fall shows no such uniform relationship to the severity of renal disease as does the extent of the urea clearance fall.

Nevertheless, in observations of nephritis, a concentration test may well be used to supplement the urea clearance for the following purposes (1) When a concentration test yields urine of more than 1.026 specific gravity, it may be assumed, as a rule, that the kidney function is normal and the clearance test may be omitted (2) In recovering acute cases, persistent low specific gravity may continue to show evidence of residual renal abnormality for weeks or months after the urea clearance has returned to normal. In assisting to decide when recovery is complete, the concentration test is therefore significant. The dilution tests yielded with nephritic patients less consistent results than the concentration tests, hence, there seemed to the authors to be no object in adding routinely a test of dilution to one of concentration. Nor did the difference between maximum and minimum specific gravity in the combined concentration and dilution test appear to be more significant than the specific gravity alone.

**Chemical Spot Test.**—High blood urea may be identified by utilizing Ehrlich's reagent (P-dimethylanilino benzaldehyde), the interaction of the two producing a yellowish-green color. A simplified technique which is adaptable to routine clinical use has been described by J. Patterson (Lancet 1:1061 (May 19) 1934) as follows:

A drop of Ehrlich's reagent is applied directly to a drop of plasma placed on a white filter paper. If the urea nitrogen is normal or only slightly elevated, there is no appreciable color change. When there is excessive nitrogen retention, however, the spot on the filter paper shows promptly the characteristic greenish color. This test has proven satisfactory for

many years at the Charing Cross Hospital in London. A further modification which is applicable to whole blood has been suggested. To 300 c.c. of Ehrlich's reagent, trichloroacetic acid is added drop by drop with shaking until the cloudiness which forms with each drop just faintly persists. A small amount of this reagent is added to an equal volume of blood, shaken vigorously, and a drop of the coagulum placed upon a white filter paper. In the presence of marked nitrogen retention, the border of the spot appears greenish and, on drying, turns bright yellow. When nitrogen is less than moderately increased, the border of the spot shows no coloration and, on drying, is a dull green.

These tests are recommended for bedside use when emergency diagnosis depends upon the immediate recognition of advanced degrees of nitrogen retention.

***Sodium Ferrocyanide as a Clinical Test of Glomerular Efficiency.***—

Ferrocyanide salts have the unique characteristic of being excreted solely by the glomeruli and for this reason have been utilized by E. J. Stieglitz and A. A. Knight (J. A. M. A. 103:1760 (Dec. 8) 1934) in a new test for glomerular function. The drug possesses the further advantages that it is nontoxic, that as a substance foreign to the body it places stress upon the kidneys, and that the variation in its excretion in normal persons is relatively slight.

*Technic*—0.25 Gm. of the anhydrous salt of sodium ferrocyanide is prepared in sterile ampoules. The contents of 1 ampoule is dissolved in 10 c.c. of sterile distilled water and slowly injected by vein. Specimens of urine are then collected at stated intervals, the times proposed being after 30, 60, 120 and 180 minutes. The urine is acidified with concentrated sulphuric acid and the amount of ferrocyanide in each specimen is estimated by titration with 0.4 per cent copper sulphate solution. As the titration proceeds, a drop of the unknown solution is placed in contact with a concentrated ferric chloride solution on a white tile and the presence of free ferrocyanide is indicated by the appearance of Prussian blue. The end point has been reached when a delay of 5 seconds or more occurs in the appearance of blue. Since 1 c.c. of copper sulphate precipitates 0.0038 Gm. of sodium ferrocyanide, the percentage of the excreted drug =

$$= \frac{0.0038 \times \text{number of c.c. of CuSO}_4}{0.25}$$

The above test was applied to a number of healthy subjects and to patients in the Cook County Hospital and very interesting results were obtained. Its degree of normal variation was found to be much less than that of phenolsulphonephthalein. In hypertensive arterial disease the excretion of ferrocyanide was considerably retarded, much more so than the phenolsulphonephthalein elimination. The authors believe that in this condition glomerular function is diminished when the diastolic pressure is raised by arteriolar hypertonia, a possibility to which support is lent by the fact that in a case of aortic regurgitation with a wide pulse pressure and a diastolic pressure of 40 mm. Hg the excretion of ferrocyanide was considerably above normal. In congestive heart failure the ferrocyanide elimination was impaired, while in known glomerulonephritis it was *nil* in severe cases or greatly reduced. The authors point out that much further work is required before the full significance of the test is understood but they feel that it offers notable potentialities for clinical usefulness.

***Phenolsulphonephthalein Test.***—It has often been shown that phenolsulphonephthalein collected from the urine in hourly specimens may give erroneous impressions as to the ability of the kidney to excrete the dye. This fact has

been emphasized by E. M. Chapman and J. A. Holsted (Am. J. M. Sc. 186: 223 (Aug.) 1933) who studied the fractional method of estimating the elimination of phenolsulphonaphthalein in 20 normal subjects and a large number of patients with suspected renal disease. The urine was collected and determinations of the dye content were made at intervals of 15, 30, 60 and 120 minutes after injection instead of at hourly intervals. It was found that in chronic interstitial nephritis the fractional test often showed evidence of impaired renal function when the test as usually done was interpreted as normal. The authors believe the fractional technic to be quite as informative as the urea clearance test and to reflect with fair accuracy the diminishing function in progressive kidney disease. Since it is easy to perform, it is recommended by them as the method of choice for routine clinical work.

**Blood Urea Clearance Before and After Urea.**—The expression of renal function in mathematical terms is probably best accomplished at the present time by means of the blood urea clearance test introduced by van Slyke and his co-workers. However, the values obtained in normal subjects cover so wide a range that they often overlap those of subjects with actual renal disease. F. S. Fowweather (Quart. J. Med. 3. 63 (Jan.) 1934) therefore made a comparison of the urea clearance test before and after the ingestion of 15 Gm. of urea in a series of patients and healthy male students. The blood urea clearance was found to be much more constant after urea than before it and in subjects without recognizable kidney disease the results occupied a comparatively narrow range, well within the original limits of normal determined by van Slyke. Fowweather concludes that the blood urea clearance after urea is a more correct indication of renal function than the values obtained before urea and recommends its routine use. It also appeared to give a more accurate indication of renal impairment in a group of patients with evidence of nephritis than both the urea and blood urea concentration tests.

**Kidney Function in Toxemias of Pregnancy.**—A comparison of the phenolsulphonaphthalein, creatinine excretion, and urea clearance tests was made by J. F. Cadden and C. M. McLane (Surg Gynec Obst 59 177 (Aug.) 1934) in 23 cases of normal pregnancy and 343 women suffering from various toxemias of pregnancy, including 216 with low kidney reserve, 90 with chronic nephritis, 9 with eclampsia, and 28 with preeclamptic manifestations. Of the 3 tests, the urea clearance alone proved sufficiently sensitive to differentiate chronic nephritis from the other toxemias of pregnancy. In the subjects without renal impairment, the lower limit for the urea clearance test was approximately 70 per cent. of normal, for nephritis the average urea clearance value was 75 per cent. of normal in antepartum cases and 68 per cent. of normal in postpartum cases. Of the nephritic patients, one-half of the total number showed values below 70 per cent. of normal. The average urea clearance values for both eclampsia and preeclampsia were definitely lower than those obtained in normal pregnancy. The authors could find no apparent relation between blood-pressure and kidney function as measured by the urea clearance nor could they demonstrate any evidence of renal impairment in the low kidney reserve group. The urea clearance test was recommended as the most sensitive method so far devised to recog-

nize early or mild nephritis, but in order to be sure that a nephritic condition is being dealt with it was advised that repeated 2-hour tests be performed.

***Creatinemia.***—The value of the blood creatinine in determining the prognosis in cases of renal insufficiency has been demonstrated by Myers and Lough. They pointed out that a rise in blood creatinine is a more important sign of renal impairment than either uric acid or urea, since creatinine is more readily eliminated by the kidney than the other products and is endogenous, while the others are exogenous. They stated that "a rise in blood creatinine above 5 mg per cent is of grave prognostic significance and portends an early fatal termination unless it is due to some acute renal condition." C. S. Higley and R. O. Bowman (J. A. M. A. 102. 1380 (Apr 28) 1934) have described 2 cases of marked creatinemia in which the creatinine level rose to 29.3 and 35.0 mg per cent., respectively, values which have only been exceeded twice among reported cases. The authors stated that the differentiation between acute and chronic renal disease is important in evaluating the prognostic significance of blood creatinine as many cases of acute nephritis may recover even after very marked creatinemia and they cite, as exemplary, a case of corrosive mercuric chloride poisoning with *recovery* in which the creatinine rose to 24.3 mg. In the 2 cases reported, the general condition of the patients appeared to be relatively good until shortly before death, despite the high creatinine values which at an early date indicated the fatal prognosis. They emphasize, therefore, the importance of regarding high creatinine values in chronic nephritis as an indication of a very grave prognosis, regardless of the patient's general condition.

***Renal Tuberculosis Diagnosis by Cultures from Urinary Sediment.***

This was studied by D. N. Eisendrath (Brit. J. Urol. 6. 37 (Mar.) 1934) and a close relationship noted between the elimination of tubercle bacilli from a tuberculous kidney and the anatomic changes incident to such an infection. To this is attributed the fact that bacilli may often be found at one examination and not at another. In a first series of 57 cases, the author obtained positive cultures from the urine in 30 but the stain showed acid-fast organisms in only 20 of the 30 cases. In a second series of 13 cases, of which 7 were proven positive by culture, the stain was positive in 4 cases at one examination and negative at another. The bladder specimen was often negative when a specimen taken directly from the kidney was positive, it was therefore considered always advisable to examine the urine obtained by ureteral catheterization. The author is of the opinion that cultures should always be controlled by animal inoculation to avoid error and should be kept under observation for at least 90 days. The culture method should be employed as a routine measure whenever the stain is negative. A smear may be made before the appearance of visible colonies in the culture, however, which is an advantage, since bacilli may be found as early as the seventh day, whereas the earliest visible colonies do not appear until the fourteenth day. It is of interest that the author was able to culture tubercle bacilli from the urine from 3 to 10 years after nephrectomy.

***Rapid Quantitative Method in Urinalysis.***—The value of a urinalysis is greatly increased by a knowledge of the rate at which formed elements are passed in the urine, as this provides an index for estimating the progress of

the renal lesion. The Addis cell count or one of its modifications is now used routinely in the majority of nephritis clinics throughout the country, but is too cumbersome for application in general practice. A simple modification has been proposed by H. Gibbons (Arch. Int. Med. 54:758 (Nov.) 1934) the technic of which may be briefly outlined. (For further details of technic, the reader is referred to the original article, where a rapid method for the quantitative estimate of albuminuria is also described.)

The patient should empty his bladder before retiring, discard this urine and note the time of doing so. The next morning the urine is passed into a collecting bottle and the time again noted. The collected urine should be well mixed and a volume equal to the number of 100 c.c. of total urine (*i.e.*, 1 per cent. of the total) is centrifuged. The supernatant urine is then carefully pipetted off. If the urine is from a 12-hour specimen, the residual volume should be 0.5 c.c., if from a 9- to 11-hour specimen, the volume must be 0.4 c.c. The sediment is then mixed with a pipette and a drop examined in a ruled blood counting chamber. The average number of elements in 0.1 c.mm. (1 small square) is counted and this number is divided by 2, the resulting figure is the number of million elements excreted by the patient in 12 hours.

Tests of this type are recommended as having a definite field of usefulness where the diagnosis is in question; a more accurate estimate of renal damage is required or the progress of the disease is uncertain by other tests. The following values are given for reference:

	casts	R B C	W B C.
Glomerular nephritis			
Initial	6,900,000	405,000,000	48,000,000
Latent	48,000	16,000,000	2,400,000
Acute	1,850,000	34,000,000	14,000,000
Terminal	398,000	26,000,000	10,000,000
Chronic nephritis	40,000	200,000	1,000,000
Nephrosis	438,000	127,000	14,000,000
Normal	5,000	1,000,000	1,000,000

**TREATMENT.—Chronic Bright's Disease.**—Current concepts of the treatment of Bright's disease have been summarized by J. P. O'Hare (J. A. M. A. 103:1373 (Nov. 3) 1934) in a general review of the subject. The term "chronic Bright's disease" includes essentially 3 diseases—chronic glomerulonephritis, chronic vascular nephritis, and chronic nephrosis. For purposes of treatment, the latter two may be considered as one disease—chronic nephritis with hypertension. The commonly accepted treatment aims at 3 primary objects: (1) the maintenance of the health of the whole body; (2) the elimination of all toxins which may increase the progress of the renal lesion, this means the eradication of proven foci of infection, the avoidance of intercurrent infections, the proper care of the bowels and a diet constructed to avoid all undue strain on the kidneys by the products of excretion, (3) the recognition and treatment of the signs and symptoms as they appear.

**Diet** is unquestionably the most important factor in treatment. In the early stages the only requirement is simple instruction to avoid an excessive intake of protein, salt and fluid. Meat and fish once a day (1 gram of protein per kilo

of body weight), no salt added to the food after it comes to the table and fluids limited to 4 pints daily is sufficiently restrictive. As the disease progresses, greater restrictions are required, but excessive protein reduction may be very harmful and should be used only when necessary and for as short a time as possible. When renal decompensation has become great, therapy is often unsatisfactory, since too rigorous protein restriction may cause breakdown of the patient's tissues and increase the toxemia, while the administration of excessive fluid may cause embarrassment to the heart. In the *vomiting* patient, an adequate amount of fluid in the form of **salt solution** or **dextrose** must be given by vein, under the skin or by rectum, and any food the patient will retain is permissible. The rest of the treatment is purely symptomatic. For the *anemia*, **Blaud's pills** may be given in 10-grain (0.6 Gm.) doses before meals, but no treatment is very satisfactory. **Transfusions** may be of transitory value in the later stages. *Cerebral symptoms in uremia* are thought to be due to intestinal toxins, so the bowels should be kept free with **cathartics** and **enemas**, with due care to prevent exhaustion of the patient. Of the sedatives, **phenobarbital** by mouth and **chloral** by rectum are recommended. For the *convulsive seizures*, **morphine** and **intravenous dextrose** are indicated and **lumbar puncture** is sometimes useful. For the extremely uncomfortable *itch*, the best remedy is **sponging with vinegar** or **weak acetic acid**.

Certain factors in treatment should be emphasized. (1) More than one-half of the patients with chronic Bright's disease die from nonrenal causes and treatment of the rest of the body must therefore not be neglected. (2) Low protein diets are often inadequate and should be used only as long as there is certainty that their advantage outweighs their harm.

In *lipoid nephrosis*, high protein **diets** are indicated for a time to replenish the lost blood protein and should be accompanied by a **restriction of salt and fluid**. Second in importance is the use of **salyrgan** supplemented by **ammonium chloride**. Less successful as diuretics are urea, calcium chloride and potassium chloride. Repeated **transfusions** may help to raise the blood osmotic pressure, but in *generalized anasarca* it may be necessary to resort to **skin incisions** or **Southey's tubes** for the removal of fluid. When lipoid nephrosis is due to syphilis, brilliant results may be obtained by **antiluetic treatment**.

Largely as a result of the speculation that Bright's disease results from spasm of the renal vessels, **diathermy** has been extensively employed in this disease for several years. A contradictory literature, however, has grown up regarding its observed effects. In an attempt to determine its therapeutic value more accurately, I. H. Page (J. A. M. A. 102: 1131 (Apr. 7) 1934) has studied the effect of 1-hour periods of diathermy on the urea clearance in 14 subjects, including patients with hemorrhagic Bright's disease, nephrosis and essential hypertension. In no case was the blood urea changed to any great extent, there being a slight tendency to fall from the first period to the last, nor was there any consistent change in the water excretion as a result of treatment. The urea clearance was not significantly altered. Blood-pressure measurements during the diathermy treatment showed no consistent change from the control level. The author concluded that these results afford no support for the assumption

that renal diathermy is of any therapeutic value in Bright's disease or essential hypertension.

**Acute Nephritis in Children.**—In a discussion of the management of acute nephritis in children, J. D. Lyttle (Pennsylvania M. J. 37: 877 (Aug.) 1934) expresses the following opinion: In nephrosis, no prophylactic treatment has been successful. **Bed rest** is important and slight activity is permissible only in the absence of edema. Sweating is ineffective and harmful; **magnesium sulphate** is the most useful cathartic. Fluid restriction is poorly borne and **sufficient water for comfort** should be allowed. The diet should be high in protein and low in salt and the appetite may often be stimulated by **insulin**. To produce diuresis, **salyrgan, potassium salts, acid-forming salts** and **urea** may be used. **Thyroid**, 10 to 15 grains (0.6 to 0.9 Gm.) daily, is sometimes helpful, but parathyroid extract has not proven successful. **Foci of infection** should be **eliminated** although this seldom appears to alter the course of the disease. Very important is prophylaxis against infections and the avoidance of exposure to cold. In acute glomerular nephritis, prophylactic treatment has proven ineffective and only scrupulous hygienic care during convalescence from scarlet fever is indicated. Milk or low protein diets are useless and harmful. In the acute stage, the patient must remain in **bed** and may be allowed up only after 4 to 6 weeks if the urine shows only minimal changes and there is no hypertension. Daily **warm baths followed by warm blankets** are preferable to sweating. For the first 48 hours the best diet is 25 per cent **glucose in water** and **orange juice** up to 1 liter (quart). Caloric requirements may be disregarded for the first 4 to 7 days and a salt-free, low protein, high carbohydrate and fat diet may be given which is increased as the blood-pressure falls. *With improvement* after 4 to 8 weeks, a **full diet** may be given. In the presence of the massive edema of a nephrosonephritis, the ordinary régime is still indicated and usually successful, although more radical treatment may be attempted for complete anuria. The more conservative measures for *oliguria* include **saline cathartics, high colonic irrigations** and **hot baths**. Uremia is very rare in children. *Hypertensive encephalopathy* accounts for half of the deaths in childhood nephritis and may be treated by **catharsis, intravenous magnesium sulphate** in 2 per cent. solution, **intravenous glucose** in 50 per cent. solution, **venesection** or **lumbar puncture**. If during the acute stage of the nephritis a pneumonia or sepsis develops or acute appendicitis, mastoiditis, empyema of the antrum or otitis, the usual surgical procedures should not be withheld, as the kidney in childhood has usually sufficient reserve to overcome the temporary ill-effects.

**Uremia.**—The effect of the experimental injection of **tissue extracts**, according to J. S. Schwarzmnn (Munchen med Wchnschr 81 1381 (Sept 7) 1934), is to reduce the rest-nitrogen in the blood, the quantity of lactic acid and the acidity of the urine, and to increase the lowered alkali reserve. From this he concluded that the relief of dyspnea which he found to follow the administration of tissue extract is due to a reduction in acidosis. On the basis of these observations, he investigated the effect of tissue extract on the dyspnea of patients with renal disease and in various forms of uremia and has reported very

favorable results. The extract was prepared from the skin, pleura and lungs, and administered by injection. Uremic attacks were usually terminated in cases of acute nephrosonephritis with varying degrees of nitrogen retention in which the manifestations included headaches, Kussmaul's respiration, nausea, vomiting and even convulsions and coma. The uremic symptoms of nephrosclerosis were also favorably influenced. To a rather lesser degree, the extract was found to be effective even in cases of chronic uremia with greatly increased nitrogen retention. The author believes that the cessation of the attacks could not have been purely accidental in view of the fact that in all his cases administration of the tissue extract was followed by definite improvement.

**Urinary Infections.**—The **ketogenic diet** is now recognized as a therapeutic measure of proven value in infections of the genitourinary tract. W. D. Goodman (M. Ann. District of Columbia 3. 195 (July) 1934) states that the diet is indicated in the following conditions: Initial or recurrent acute pyelonephritis or cystitis without acute obstruction, chronic urinary infection without demonstrable gross pathologic changes, chronic urinary infection associated with pathologic changes demonstrable by x-ray or cystoscopy, urinary infections following operations, preliminary preparation for certain urologic operations, urinary infection following instrumentation, urinary infection following gonorrhea, and in the presence of inoperable neoplasms and anomalies of the genitourinary tract. The author obtained satisfactory results in 21 of 30 cases receiving the diet, 5 of which were outstanding cures. Local treatment, however, must be given for foci of infection and vitamins should be added to prevent metabolic disturbances. If *ketosis becomes too severe*, the condition may be relieved by giving a small amount of **orange** or **tomato juice**. Patients on the diet may lose from 4 to 10 pounds and it is generally not well tolerated by thin, cadaveric subjects.

D. C. Robb (Brit. M. J. 2. 1158 (Dec. 23) 1933) reported the effect of the ketogenic diet in 16 cases of infection of the urinary tract. An increase was produced in hydrogen ion concentration of the urine in all cases except one. The effect of the urinary pH was characterized by a rapid initial fall and a maintained low general level lasting until the end of the third week, when a tendency was found for the pH to become irregular and to stand at a slightly higher level. Acetone bodies were produced in the urine in all cases but varied greatly in amount in individual cases. Acetone appeared in greatest amount during the first 5 days after the pH had fallen and by the end of 3 weeks became very much diminished. Five patients were cured completely by treatment with the ketogenic diet, the pH remaining about 5.4, four patients were cured following the addition of **ammonium nitrate**, and 2 following the addition of **methenamine**. No symptoms were caused by the hyperacid urine. It was found preferable to increase the diet by stages according to the ketogenic/antiketogenic ratio, in order to avoid nausea and vomiting, and only 1 patient had any gastric upset on this régime. Every patient was in excellent health on discharge from the hospital.

**Nephritis.**—An exclusive **sugar diet** has been used with success by Z. von Bokáy and L. von Kostyál (Arch. f. Kinderh. 100. 123 (Sept. 29) 1933) in the



treatment of acute nephritis. For a number of days until improvement set in, the patients were given from 250 to 400 Gm. (8 to 13 ounces) of malt sugar or potato sugar and nothing else. Thereafter, fruit and a little water were added until gradually a mixed diet was again introduced. The treatment was employed in 50 cases of which acute hemorrhagic glomerular nephritis occurred in 34, subacute hemorrhagic nephritis in 4, chronic nephritis in 5, nephrosis in 6 and scarlet fever nephritis in 1 case. The patients with acute nephritis recovered in 16 days or less; those with chronic nephritis or nephrosis recovered in from 15 to 30 days. The authors believe that an exclusive sugar diet rests the kidneys and thus promotes recovery. The favorable effect of the sugar diet is attributed partly to the result of a direct action on an intermediate metabolism and partly to an indirect action by way of the liver. The sugar diet also appeared to influence the disturbed water exchange that exists in renal inflammations. It favors a reduction of the osmotic pressure of the blood, an increase in perspiration, and a reestablishment of the renal and extrarenal elimination of water.

**Suppurative Nephritis.**—L. Moriconi (Clin. chir. 37:637 (July) 1934) studied the effect of **bilateral decapsulation of the kidney** and of **bilateral sympathectomy of the renal artery** on the appearance and evolution of suppurative nephritis. The disease was produced artificially in dogs by intravenous injections of a culture of staphylococcus tropicus. By the tenth day after operation the author observed a marked increase in the elimination of urine, with concomitant renal hyperemia. The increased flow of urine and the accompanying hyperemia did not appear, however, to be of any value in the prevention of the experimental nephritis. The advantages of the operation were believed by the author to lie in the increase of the local defense power of the kidney and not in the greater facility for the elimination of microorganisms through the increased excretion of urine or in the accompanying hyperemia. The functional activity of the kidney was found to be increased and the procedure, therefore, concluded to be of definite value.

**Effect of Sympathectomy in Experimental Nephritis.**—Numerous studies have been made of the nerve supply of the kidney to determine whether various nervous factors are of any importance in the treatment of renal conditions. E. Ruggieri and G. Bazzocchi (Arch. ital. di urol. 10:381 (July) 1933) have reported experiments which were carried out on rabbits to determine the behavior of the nephritic kidney after periarterial sympathectomy, particularly as regards acute lesions. After periarterial sympathectomy had been done on the left renal artery, the animals were given 1 or 2 intramuscular injections of uranium nitrate solution followed by adrenalin which produced a fatal glomerulonephritis. At various intervals after the injections, the kidneys were removed and studied histologically. In the kidney which had been operated upon, the parenchymatous lesions were usually much less severe than in the intact organ. In the light of these results the authors believe that sympathectomy exerts a protective action on the kidneys against the damaging effects of the uranium.

**Anuria.**—**Peritoneal Dialysis.**—Intravital dialysis of the blood has been therapeutically applied by J. Balazs and S. Rosenak (Wien. klin. Wchnschr. 47:851 (July 6) 1934) in cases of *poisoning with corrosive mercuric chloride*

The technic consisted of the performance of a buttonhole laparotomy at the upper median line of the abdominal wall and in the ileocecal region. Through each of these openings a perforated glass cannula was introduced in such a manner that the end of one cannula came between the liver and the diaphragm and the end of the other into Douglas' pouch, making possible a continuous irrigation of the abdominal cavity. Irrigation was maintained for 3 to 4 hours with a 4.2 per cent. **dextrose solution**, which appeared preferable to sodium chloride solution. The temperature of the irrigating fluid was kept between 42° and 45° C. Peritoneal dialysis is recommended by the authors in the presence of severe anuria or oliguria resulting from poisoning with corrosive mercuric chloride, particularly when uremic symptoms threaten, and was found to give excellent results in such cases. It may be combined with **infusion** and **venesection**.

**Postscarlatinal Nephritis.**—**PROPHYLAXIS.**—The value of **tonsillectomy** as a prophylactic measure in postscarlatinal nephritis has been subjected to investigation by A. A. Osman (Guy's Hosp Rep 84 210 (Apr) 1934). With the cooperation of the Infectious Disease Service of the London County Council, 10,000 cases of scarlet fever occurring during 1 year were reported as to the occurrence of albuminuria or nephritis and whether or not previous tonsillectomy had been performed. Nephritis was defined as "any condition in which blood is detected in the urine." Of the 10,000 cases of scarlet fever, 21.27 per cent had had previous tonsillectomy, while 78.6 per cent had not, of the patients developing nephritis, 1.2 per cent had had previous tonsillectomy and 1.74 per cent had not, and of the patients exhibiting albuminuria, 5.7 per cent had had previous tonsillectomy and 4.6 per cent had not. The total incidence of nephritis was only 1.74 per cent for the entire group, while the incidence of albuminuria was 4.84 per cent. For this reason Osman was forced to the conclusion that tonsillectomy is without value in diminishing the incidence of postscarlatinal nephritis. He believes that although it cannot be argued that prophylactic tonsillectomy is equally without value in posttonsillitic nephritis, the increasing number of such cases in whom this operation has been performed at some time prior to the onset of nephritis suggests that this will prove to be the case.

Continuing his study of postscarlatinal nephritis, Osman (*Ibid* 84 302 (July) 1934) also attempted to estimate the prophylactic value of giving **antiscarlatinal serum**. The total number of cases of undoubted scarlet fever was 11,282, of which 26.8 per cent received antiscarlatinal serum and 71.4 per cent did not. Of the entire group, 1.7 per cent developed nephritis. Of the patients who received serum, 1.58 per cent developed nephritis and of those who did not receive serum, 1.56 per cent developed nephritis. Osman considered the possible sources of fallacy in such a study but was unable to escape the fact that there was no significant difference in the percentage of serum-treated patients who developed nephritis from patients not treated with serum in whom nephritic manifestations occurred. He concluded, therefore, that "antiscarlatinal serum is of no value in the prevention of postscarlatinal nephritis."

**Phases of Kidney Disease Indicating Abortion.**—W. W. Herrick (J. A. M. A. 103 1902 (Dec. 22) 1934) states that an understanding discussion of abortion in relation to disorders of the kidney calls for classification into various

clinical and pathologic types and a consideration of each in its relation to pregnancy. The *toxemias of pregnancy* seem to fall into 2 groups. The first and smaller group includes the nephritides, the outstanding feature of which is prolonged and marked albuminuria with a tendency to anemia, edema and uremia; hypertension is not obligatory. Cases of this kind do badly in pregnancy and usually require abortion when nephritic symptoms are manifest and do not yield to treatment. *Repeated pregnancies* are practically always unfortunate in outcome, leading to fetal death and acceleration of the downward course of the disease in the mother. The larger group of toxemias seems to include *eclampsia*, *pre-eclampsia*, and the larger number of milder disturbances variously classified under such terms as "*recurring toxemia*," "*nephritis*" and "*substandard kidney*." The dominant feature of this group is hypertension. Nitrogen retention and uremia do not occur except rarely as the end-result of renal arteriosclerosis. Albuminuria is usually absent. In this group the problem of abortion is usually less urgent than in the nephritic group. In the acute eclamptic cases abortion is usually unwise, as it adds greatly to the maternal burden at a most critical time. Recovery with continuation of pregnancy or the more frequent event of fetal death and spontaneous delivery with relief of toxic symptoms may be looked for in all excepting the 15 per cent of mothers who die in the acute attack. Except in particular cases with special features, conservative medical treatment is safest. In the less acute types the decision as to abortion may be made in more leisurely fashion. If hypertension appears early in pregnancy and increases despite treatment, abortion is indicated. When to hypertension are added albuminuria and edema not yielding to treatment, the same action is advisable. If viability of the fetus can be obtained by delay, this may be risked in selected cases under careful supervision. The adverse effect on maternal health of the prolongation of pregnancy under these circumstances must always be borne in mind, there is no better recipe than this for the production of chronic vascular disease. Repeated pregnancies are to be discouraged, except in mild cases, appearing late in pregnancy and usually with little or no albuminuria or edema. Some of these do not recur when reproduction is again attempted. However, it must be emphasized that each case is an individual problem to be solved on its own merits.

**Nephrosis.**—Studies of the effect of a **high protein diet** on small groups of patients with nephrosis were made by G. Czoniczer and S. Weber (Klin Wchnschr 12 1566 (Oct 7) 1933) who found that the characteristic hypalbuminosis could not be definitely influenced by a diet rich in proteins given over periods of from 4 to 10 days. The daily excretion of protein of the same nephrotic patient was found to be constant and characteristic for this patient for a certain stage of his disease. The addition of 180 Gm (6 ounces) of protein per day to the diet caused an increase of 40 to 100 per cent in the urinary protein excretion. The urinary output, however, was distinctly increased by a high protein diet, in the presence of edema the volume of fluid excreted exceeded that taken in with resultant decrease in the body weight. It was concluded that because of increased diuresis and reduction of edema, high protein diet is indicated in pure lipoid nephrosis and in the nephritides. The increase in albuminuria is of slight importance and there is no need to fear retention of nitrogen.

**Renal Calculi.—Glycerin Therapy.**—Many therapeutic procedures are of value in the elimination of renal calculi and among these F. Lickint (Munchen med Wchnschr 81 821 (June 1) 1934) includes **ureteral massage, dilatation of the ureters**, flooding of the urinary passages by the administration of **large amounts of fluid, hypophyseal extracts** for the stimulation of peristalsis and the use of **volatile oils**. Superior in many respects, however, is the administration of **glycerin** in large doses, by which treatment he obtained expulsion of the stone in 14 of a series of 16 cases. Following a discussion of the part played by glycerin in normal metabolism and the elimination of glycerin following its administration, he describes its mode of action in expelling calculi, this consists of a spasmolytic action, a stimulating effect on peristalsis, a diuretic effect, an increase in the density and viscosity of urine, and a facilitation of expulsion by dissolving and diminishing the calculi. The author points out that small doses will result in failure and he advises the administration of 50 c c (1 $\frac{1}{2}$  ounces) of glycerin 3 times daily for 3 successive days. No undesirable effects in his cases have resulted from this régime and the treatment is highly recommended in view of the favorable results obtained in the majority of cases.

**Treatment of Renal Complications of Hyperparathyroidism.** Among 83 cases of hyperparathyroidism studied by F. Albright, P. C. Bard, O. Cope and E. Bloomberg (Am J M Sc 187:49 (Jan) 1934) 43 developed renal complications, due to the precipitation in the kidney of calcium phosphate. Precipitation in the renal pelvis resulted in pyelonephritis, precipitation in the renal tubules resulted in renal sclerosis, contraction and insufficiency, precipitation in the kidney as well as in other organs often resulted in acute renal failure or death of unknown cause in a few hours or days. It was pointed out that hyperparathyroidism should always be suspected in the presence of a renal stone and that in severe cases the renal lesions of the disease may occur without bone changes. The *prophylactic* treatment for preventing renal damage in hyperparathyroidism includes **forcing fluids** and the **avoidance of an alkaline urine**. Ammonium chloride and other acid-producing salts are contraindicated. Although a high phosphorus diet may be indicated for demineralization, it should be used with caution since it is harmful to the kidneys, a high calcium diet is likewise undesirable. The authors reported a case where improvement in the bone condition followed medical therapy for hyperparathyroidism, but where kidney damage eventually occurred and they believe that most patients with this disease will sooner or later develop kidney damage which may be avoided by timely recourse to **parathyroidectomy**.

Three cases of *parathyroid adenoma* complicated by renal calculi were reported by F. H. Colby (Surg Gynec Obst 59:210 (Aug) 1934) who emphasized the fact that tumors of the parathyroid gland cause metabolic disturbances which result in marked increase in urinary output of calcium, decrease in output of phosphorus and sometimes lead to formation of stones in the urinary tract. Like the preceding authors, he found that calculi may be formed without the characteristic bone changes to indicate the presence of the parathyroid tumor, the underlying cause of the stone formation. In his experience, stones may continue to recur unless the parathyroid tumor is **removed**.

# Diseases of Metabolism

*by*

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**DIABETES.—Complications.—Cataract.**—This is a well-recognized complication of severe diabetes mellitus in young persons, but it is considered to be comparatively rare. It is believed by some to occur only in those cases with associated vascular disease. In its typical form diabetic cataract is described as developing in both eyes with great rapidity, *i. e.*, within a few hours or days. There is no evidence of a characteristic morphology; different observers describe subcapsular vacuoles, water slits, and various types of grayish white and iridescent subcapsular and cortical opacities; for example, reticulate, asbestos-like, punctate and flocculent. Also a saucer-like gray and opalescent posterior subcapsular opacity is described. C. S. O'Brien, J. M. Molsberry and J. H. Allen (J. A. M. A. 103:892 (Sept 22) 1934) present a study of the crystalline lenses in young diabetic subjects, which was undertaken in order to determine the incidence and morphology of cataracts in such patients. The report is founded on repeated detailed examinations, with the slit lamp microscope, of the lenses in 126 diabetic patients up to and including the age of 33 years. Most of the patients, when first seen, had been under treatment for some time. Practically every lens in the entire series showed occasional small punctate congenital cataract was present; the diagnosis in such cases was usually not difficult, but in those lenses in which doubt existed, the changes were classified as congenital.

Severe, prolonged, poorly-controlled diabetes was present in many of the 126 cases and, with but 2 exceptions, in 20 cases presenting complicating cataracts. According to the histories, the duration of the general disease, at the time lens opacities were detected, varied from 1 to 13 years, the average being approximately 5 years. The severity of the diabetes in patients with cataracts was indicated by the high concentrations of the blood sugars and glycosuria in 18 of the 20 cases, and the invariable evidences at one time or another of ketonemia and ketonuria. The blood sugars, on admission to the hospital, varied from 170 to 700 mg per 100 c.c., the average concentration being 373 mg. Evidences of ketone bodies in the urine were found in every patient; in 3 cases there was a history of coma. These conditions were present despite efforts to restrict the diet and advice as to the use of insulin, showing the difficulties in the home control of diabetes. In many of the patients other pathologic conditions of more or less severity were known to have been present or were discovered at the time of examination, but in no case were they of a type known to cause cataract. Arteriosclerosis was found in only 1 patient.

A diagnosis of diabetic cataract was made in 20 of 126 cases, an incidence of 16 per cent. There were 13 males and 7 females affected. The lenses were normal in 31 patients under 11 years of age; opacities were present in 8 of the 58 patients aged from 11 to 20 years, inclusive; in 9 of 31 patients aged from 21 to 30 years, inclusive; and in 3 of 6 patients aged from 31 to 33 years, inclusive. These changes were bilateral, with 1 exception, in 1 patient, opacities were just forming in 1 eye and evidently had not begun in the other. It is recognized that diabetic cataract may form and mature within a few days, but the development of lens opacities in the cases herein reported was not extremely rapid; in most instances it was a matter of weeks or months.

Only a small number of lenses had been studied when it was realized that there were 2 common types of cataract. The more unusual and striking of the two was that designated as *snowflake* or *snowstorm cataract*; it appeared first in the anterior and posterior cortical areas, near to, but not immediately under, the capsule, as innumerable scattered grayish to bluish-white flake opacities. In later stages the opacities occupied the entire cortex. The appearance with the biomicroscope was that of a heavy snowfall against a leaden sky. This snowstorm cataract was seen in 12 cases, an incidence of 60 per cent. It was well-developed and typical in 10 cases, and appeared in slightly atypical form in 2 cases. There is reason to believe that such opacities may have been present in other lenses during early stages of development of the cataract.

The common type of cataract was a *saucer-like posterior subcapsular opacity* of confluent gray granules and oftentimes containing iridescent crystals. Frequently, finely granular, radial, posterior subcapsular striæ extended from the equatorial zone toward or into the central opacity. This is not an unusual type of opacity, since it appears following injury, in association with certain ocular diseases and occasionally as a senile lens change. It was present in its typical form in 12 cases and in an atypical form in 2 cases, an incidence of 70 per cent.

*Anterior subcapsular opacities* were found in 8 cases, an incidence of 40 per cent; they were punctate, finely granular or veil-like, and occasionally showed iridescent crystals. In some lenses delicate radial striæ were present.

*Iridescent crystals* were noted in 8 cases, an incidence of 40 per cent. They were usually located in the subcapsular areas, but in a few lenses were found in the cortex.

It is to be understood that more than one type of opacity was present in many lenses and that vacuoles, water slits and lamellar separation were common changes.

*Hyperthyroidism* -- A case is reported by R. G. Hills, J. C. Sharpe and L. N. Gay (Bull. Johns Hopkins Hosp. 55: 193 (Sept.) 1934) that presented the symptoms of mild diabetes and mild hyperthyroidism. The patient had had diabetes during the 3 previous years, hyperthyroidism had come on apparently 2 months before. Twenty-four hours after the patient knew that she was to be operated on, hyperglycemia and ketonuria developed in spite of precisely the same regimen that had controlled the diabetes during the 8 preceding months. Extreme fear had apparently precipitated an exaggeration of the hyperthyroidism, and this, in turn, had caused a decrease of sugar tolerance. After 6 days of preoperative treatment, marked hyperglycemia persisted. A subtotal thyroidectomy was performed. Following the operation, sugar tolerance was markedly decreased, necessitating the daily administration of from 200 to 890 units of **insulin**. Compound solution of iodine given for 4 days was without benefit. Irradiating the pituitary was considered, but the x-rays showed that the sella turcica was smooth in outline and only slightly larger than normal. The onset of bronchopneumonia and a urinary tract infection produced a marked ketosis, which necessitated 890 units of insulin in 24 hours. The intravenous injection of **sodium bicarbonate** brought about a subsidence of the acidosis. The sugar tolerance increased rapidly following the resolution of the pneumonia. However, vascular collapse and repeated



insulin shocks were followed by cerebral thrombosis with hemiplegia and aphasia. After this, the patient improved gradually. Contrary to the experience of John, Joslin and Lahey, who point out that thyroidectomy lowers total metabolism and consequently improves the carbohydrate tolerance, the patient showed no improvement. She was refractory to insulin before the removal of her thyroid, but not until after the emotional disturbance precipitated by her decision to undergo thyroidectomy. When she left the hospital, twice as much insulin was required to control the diabetes as had been necessary before the thyroidectomy. The cause of the ineffectiveness of insulin was not determined.

*Insulin Sensitivity.\**—There have been increased numbers of cases of allergy to insulin reported in the literature during the past several years. L. M. Bayer (J. A. M. A. 102.1934 (June 9) 1934) reports a case of sensitivity which developed in a woman of 48 in whom there was no family history of diabetes. She first took insulin in 1932 and stopped it after a few months without showing any allergic reactions. In April, 1933, she was again started on insulin and within a few weeks noticed a gradually increasing occurrence of wheals at the sites of injection. This condition was present regardless of the commercial preparations employed, and on one occasion following 5 units of insulin she developed in 20 minutes violent abdominal cramps and a macular itching rash over the whole body, also diarrhea and a sense of choking. Her skin tests showed pseudopods and hyperemia following the injection of 0.01 c c of 4 commercial preparations of insulin. A desensitization program was planned in which U-40 insulin was made up with distilled water to suitable dilutions and Chart I shows very clearly the technic and result of this rapid desensitization process.

CHART I  
DESENSITIZATION PROCESS

Units	Time	Reaction
1/100	9 15 a. m.	++
1/100	9 45	++
Sterile distilled water	9 47	0
1/200	10 16	+
1/200	10 46	++
1/400	11 20	++
1/1,000	11 42	+
1/1,000	12 20 p. m.	±
1/500	1 30	+
1/250	2 03	±
1/125	2 32	±
1/66	3 04	±
1/50	3 36	0
1/25	4 02	0
1/10	4 16	±
1/5	4 30	±
1/2	4 45	±
1	5 01	0
5 (hypodermically).	5 20	0

++ denotes wheal of at least 1 cm. with surrounding hyperemia, +, wheal of less than 3 mm. with surrounding hyperemia, ±, no wheal, faint hyperemia, 0, no reaction

\* See also Section on ALLERGY

In commenting on insulin allergy, Bayer points out that this particular case, as in many of the others reported, had no allergic history and he advances the thought that insulin allergy is an acquired state similar to drug and serum allergies. This case did not show sensitization when insulin was first given, but it came on gradually and increasingly, and particularly after the use of insulin. The patient showed both the local and general reactions which are apt to occur. The method described by Bayer seems very simple and safe to use for desensitization of any patient so effected.

J. A. Murphy, J. T. Beardwood and M. M. Miller (J. Allergy 5: 606 (Sept.) 1934) report 2 cases of insulin sensitivity with an attempt of passive transfer. Both these patients developed allergic reactions on the seventh day after the primary dose. A change in the brand of insulin brought relief to one but not to the other. The attempt of passive transfer failed. The major reaction in these 2 cases varied, one showing generalized urticaria and the other, asthma.

*Cancer*—Until comparatively recently, the association of cancer and diabetes was thought to be rare. Lately, however, there has been an increasing incidence, possibly because diabetics are living into the "cancer age." A Marble (New England J. Med. 211: 339 (Aug. 23) 1934) made an analysis of 256 cases in which malignant disease and diabetes were associated, representing cases recognized among 10,000 diabetic patients. Among the fatal cases, the average duration of diabetes was 7.1 years. The average duration of symptoms of cancer was 1.8 years. The conclusion is drawn that, in general, cancer develops in the diabetic and not diabetes in the patient having cancer. Evidence is lacking that cancer brings about the diabetic condition. A study of available data shows that the increasing percentage of cancer deaths to total deaths during the last two decades is greater among diabetic patients than among members of the general population. This is thought to be due, in part at least, to the fact that the increased longevity of diabetic patients during the last decade has placed relatively more diabetic than nondiabetic persons in the cancer age zone. It does not necessarily imply, however, that the diabetic patient is any more likely to develop cancer than the nondiabetic person. The author's series includes 33 cases of *carcinoma of the pancreas*, 21 having been diagnosed either at operation or at necropsy. The incidence of carcinoma of the pancreas was therefore extraordinarily high. It was 12.9 per cent. of the total number of cases, as contrasted with less than 5 per cent. in the general cancer statistics reported by others. The average duration of symptoms of cancer in the 21 proved cases of carcinoma of the pancreas was 1 year, in these cases the average duration of diabetes was 3.4 years. The latter figure represents the shortest duration of diabetes of any group of diabetic patients under observation. Thus, a possible relationship between cancer of the pancreas and diabetes is suggested. Figures from the literature, however, tend to indicate that diabetes is relatively uncommon in cases of carcinoma of the pancreas.

*Tuberculosis*.—J. J. Wiener and J. Kavee (Am. Rev. Tuberc. 30: 181 (Aug.) 1934) treated 26 cases of active pulmonary tuberculosis complicated by diabetes mellitus with **artificial pneumothorax**. The cases chosen for treatment had active pulmonary tuberculosis with tendencies to progression and, with a single

exception, were febrile. The age incidence of the patients closely approximated that observed in diabetic patients in the general population. In 19 the left and in 10 the right lung was collapsed. This number includes 1 in whom a bilateral pneumothorax was induced. The lesions were in the main those which have been described as the type best elicited with the aid of the x-rays. In the 26 cases, marked immediate improvement was noted in 9, slight symptomatic improvement in 5, and no improvement in 12 cases, in 3 of which a free pleural space could not be found. The 9 patients who showed marked immediate improvement are still alive and in excellent condition. Of these cases, 6 had bilateral lesions. They have been well for periods varying from 20 months to 9 years. Of the 5 patients in whom only slight symptomatic improvement was noted soon after the initial induction, 4 died within a period of from 5 to 19 months and 1 could not be traced since leaving the hospital. Eleven of the 12 patients who showed no improvement died within 1 and 20 months after the induction. The other patient did not improve at first, but subsequently, after the appearance of a massive effusion collapsing the lung quite completely, the course being afebrile and the disease quiescent. Improvement was often dramatic, with cessation of hemorrhage, decline of fever, and diminution of cough and quantity of sputum. The usual complications that occur following collapse therapy were observed just as frequently as in nondiabetic tuberculosis patients.

**Diagnosis.**—**DEXTROSE TOLERANCE TEST** —A new type of dextrose tolerance test is reported by W. G. Exton and A. R. Rose (Am. J. Clin. Path. 4: 381 (Sept.) 1934) which seems to offer some advantage in that the time is shortened and the number of blood sugar determinations made is only three. It would seem to be a test which might be more readily used in office practice.

**Technic** —One hundred grams of dextrose is dissolved in about 650 c.c. of water. This solution is flavored with lemon and divided into 2 equal doses, which are served cold. Three containers with preservative against glycosuria are kept at hand for the blood specimens and 3 containers for the urine specimens. When collecting the specimens, the subject should empty the bladder as completely as possible. The following steps are taken after a fast, preferably over night. The samples of blood and urine are collected and the first dose of dextrose is given, from 1 to 2 minutes being allowed for its ingestion. Thirty minutes later, samples of blood and urine are collected. The third urine container is given to the subject for a sample of the urine next voided whenever a (post) sample is desired. When the results of the foregoing procedure are plotted, the interpretation of the first part of the curve, *i. e.*, the part that includes the original and 30-minute samples, is exactly the same as the interpretation of the same part of the curve of the older procedure, and the same deductions are drawn accordingly from the blood and urine sugar values. Interpreting results of the second part of the 1-hour 2-dose tests indicates that normal subjects respond to the second dose of dextrose with a greater fall in blood sugar than that occurring during the same period after only a single dose and there is no sugar in the urine. The criteria for determining diabetes in the 1-hour 2-dose test are a more or less steep rise of not less than 10 mg. of blood sugar in the 60-minute sample following the second dose of dextrose and the relation of the blood and urine sugar values to the severity of the disease. The criteria for the test of renal glycosuria are blood sugars that follow the normal course, or in any event never reach the diabetic level, and sugar in both urine specimens. The criteria of alimentary glycosuria are: a sugar-free urine after fasting with sugar in the final urine and blood sugars that follow the normal curve even when the level is higher than normal.

Up to the present time the authors have not encountered a single instance in which the new test disagreed with the older when the results of the older test were satisfactory. On the other hand, many cases have doubtful or misleading responses to the older test when results of the new test were consistent and specific.

The results of the sugar tolerance tests in siblings of juvenile diabetic patients are reported by H. S. Mackler and A. E. Fischer (J A M A. 103. 240 (July 28) 1934). They quote the work of Pincus, White and Joslin on the familial or hereditary character of diabetes and the work of Cammidge, who has presented an experimental proof of the clinical work just cited. This study was undertaken with the idea of following the siblings of diabetic children under the authors' care for some time after the dextrose tolerance test had been studied. Thirty siblings of 20 diabetic children were studied; 20 were Jewish and 10 non-Jewish. Twenty of the 30 were examined in 1934.

*Technic*—The Kuttner modification of the micro-Folin-Wu test for blood sugar was used. All estimations were made on capillary blood soon after its withdrawal. Studies were begun after a 14-hour overnight fast. Determinations for dextrose were done on the samples withdrawn in the fasting state and at intervals of  $\frac{1}{2}$ , 1,  $1\frac{1}{2}$ , 2 and  $2\frac{1}{2}$  hours after the ingestion of the dextrose solution. The amount of dextrose to be used was estimated by means of the formula devised by Pirquet. This utilizes the sitting height squared as the index of the nutritional surface area. Fries and Kohn found this method to be satisfactory for estimating the dextrose to be administered when determining the sugar tolerance curve in children. In terms of grams of dextrose per kilogram of body weight, this amounted to from 0.96 to 1.85 Gm per kilogram of body weight. Gilchrist found that the blood sugar curves in children, when given 1 Gm or more of dextrose per kilogram of body weight were similar to those found in adults.

The siblings of the diabetic children were on the whole slightly overheight and overweight when compared to average normal standards. In only a few instances, however, was overgrowth striking.

Of thirty sugar tolerance tests, 25 were normal, 3 had a relatively high figure at the 1-hour reading, and 2 of these were still high after  $1\frac{1}{2}$  hours. All 5, however, were normal after the  $2\frac{1}{2}$ -hour period. It is interesting to call attention to the fact that in 16 instances the  $2\frac{1}{2}$ -hour reading was below the fasting blood sugar. This phenomenon has been observed by others in normal individuals. No indication of decreased tolerance was noted in a girl whose 2 brothers and 1 sister have diabetes. Subject 9, who was recuperating from an acute mastoiditis at the time of the test, had a curve within normal limits. One of heterozygous twins, L. T., showed a rather high curve, her blood sugar at the end of  $1\frac{1}{2}$  hours being 140 mg. This child, as well as M. T., her twin sister, was retested early in 1934. Their curves at this time were both normal. L. T.'s fasting blood sugar was 65 mg, which rose to 120 mg at the end of  $1\frac{1}{2}$  hours and fell to 75 mg at the end of 2 hours. M. T. had an even lower curve.

It was with particular interest that the urine of the siblings was reexamined in 1934, 6 years after the dextrose tolerance tests. Urine was obtained from 21 of the 30 children whose curves are tabulated, including the 5 who had slightly elevated sugar tolerance curves. No glycosuria was found in any of the specimens. All 3 children who were more than 5 per cent. overheight for their age,

had normal blood sugar tolerance curves when they were reëxamined. In addition to being siblings of a diabetic child, they were markedly overgrown, but as yet have shown no indication of diabetes. They intend to repeat the dextrose tolerance tests of all these siblings after a few more years.

In the series of 57 juvenile diabetic patients, some of whom have been observed for as long as 9 years, no brother, sister or parent developed diabetes during that time. In some instances, to be detailed in a subsequent paper, a close relative became diabetic. Since 9 years is only a fraction of the average life expectancy, these observations are of limited significance, for siblings and parents of juvenile diabetic patients may develop diabetes at any time over a period of years. It was hoped, however, as indicated by other workers in this field, that it might be possible to detect a predisposition to diabetes by means of the sugar tolerance test. This has not been the case thus far in 30 siblings of juvenile diabetic patients, as indicated by the curves as well as the subsequent histories of these patients. Since the onset of diabetes in children and in adolescents is, as a rule, rather sudden, they feel that the sugar tolerance method does not hold much promise as a means for detecting early cases of diabetes in childhood. This method might be of value in older patients in whom the onset of diabetes is frequently insidious.

*Differential Diagnosis*—The differential diagnosis of *renal diabetes* and diabetes mellitus is often one which the physician is called upon to make. Solomon Silver and Miriam Reiner (Arch Int Med. 54:412 (Sept ) 1934) report their observations in 3 cases of essential alimentary fructosuria, and from their careful studies they feel that essential alimentary fructosuria is a specific, probably inborn, error of metabolism, characterized by the inability of the organism to utilize fructose normally and manifested clinically by a symptomless excretion of fructose. Fructose is passed in the urine only if fructose or a substance capable of yielding it on digestion are ingested. All the reducing substances disappear from the urine if these foods are removed from the diet. The usual sources of fructose are cane sugar, honey and fruit. This disorder is not inconsistent with longevity and there is no reason to believe that it is a precursor of a diabetic state. Transition from fructosuria to glycosuria has never been observed. The tolerance and metabolism of all the other known carbohydrates are normal in this condition. Dextrose, taken orally by the patient whom the author studied, gave only the expected rise in blood sugar and caused no glycosuria, and the hyperglycemia reached the fasting level by the fourth hour. Galactose was tolerated in a normal dose of 40 Gm. (1½ ounces). The relative significance of insulin and epinephrine in the metabolism of fructose compared with dextrose is pointed out and the possible intermediary metabolism of sorbitol is discussed.

S R Salzman (J A M A 103 483 (Aug 18) 1934) reports a case of *pentosuria* which had been followed for 13 years. This patient was seen at varied intervals by the writer and by other physicians, and her metabolic condition was well studied. Although on several occasions the reducing substance in the urine was thought to be dextrose, a diagnosis of renal diabetes was made. Salzman was able to show that the sugar excreted was pentose, and as the patient was in excellent health and her physical development in no way retarded, he

concludes that pentosuria is essentially a harmless anomaly and stresses the importance of attempting to diagnose this condition in all cases of renal diabetes.

What is not stressed in this report, but which is important to remember, is that the diagnosis of renal diabetes should not be made until the patient has been observed for some time, preferably over a period of years, since not infrequently cases so diagnosed will become cases of frank diabetes later on.

**Treatment of Coma.**—In treating dehydration of neglected diabetic coma, F B Byrom (Lancet 1 446 (Mar. 3) 1934) treats the case as one of profound shock. The patient must be kept **warm**. Immediately after admission he is given from 50 to 100 units of **insulin** intravenously, followed by 500 c.c. of warm **physiologic solution of sodium chloride**. Meanwhile, **dextrose**, to last the patient for 24 hours (usually about 500 Gm.— $16\frac{2}{3}$  ounces), is dissolved in about 2 liters (quarts) of half strength physiologic solution of sodium chloride, which is given to the patient by mouth in 24 equal doses, accompanied by subcutaneous injections of suitable doses of insulin. As a rule, from 10 to 20 units is injected every hour until the blood sugar, which is estimated hourly, has fallen to normal. The patient is encouraged to drink freely half-strength physiologic solution of sodium chloride. When this solution is used, both salt and water are almost quantitatively retained and little is excreted. The dextrose and saline mixture is well tolerated by the patient and seems less prone to cause vomiting than dextrose dissolved in water. It should be given in small mouthfuls. If the patient cannot be roused after the first intravenous injection, care should be taken, if further infusions are necessary, to see that the fluid is injected slowly enough to permit diffusion into the tissue spaces without burdening the heart. This routine should be suspended as soon as clinical evidence of dehydration disappears.

The use of **hypertonic salt solution** in diabetic coma is stressed by H F Root (J A M A 103 482 (Aug. 18) 1934). He states that deaths from diabetic coma are frequently accompanied by anuria, developing 6 to 12 hours before death. In the aged patient this sometimes may be due to a chronic nephritis, but in the young it is usually regarded as due to renal block caused by the acidosis and fall in blood-pressure. In certain cases vomiting, especially in children, may continue after acidosis, as indicated by the presence of diacetic acid in the urine, has disappeared. The renal irritation due to diabetic coma, as shown not only by the typical coma casts but also in many cases by leukocytes and even red blood cells, may persist and, indeed, may explain the vomiting as in the other case here reported. The effect of dehydration and loss of chlorides due to vomiting must not be overlooked and it is important to investigate the level of the plasma chloride in each case of anuria, since in some instances the administration of hypertonic salt solution is life-saving. Root cites 3 cases in which the plasma chlorides were depressed and anuria was present. Fifty to 60 c.c. ( $1\frac{1}{2}$  to 2 ounces) of 10 per cent. saline solution were given intravenously, which was followed by the passage of urine and a return to normal kidney function. He feels that in all cases which do not react promptly to the usual treatment or in which anuria develops, hypertonic salt solution should be used.

*In Children.*—H. J. John (Am. J. Digest. Dis. and Nutrition 1:180 (May) 1934) presents his experiences with the diagnosis and treatment of diabetic acidosis and coma in children. In a series of 218 diabetic children coma occurred in 50 cases, or 23 per cent., over a period of 13 years, and these were divided into 2 groups: (1) Those that were under the writer's immediate care during the coma and this group comprised 31 cases; of these, 5 died, 1 in the pre-insulin era; 3 were moribund on admission and died within 1 hour. If these 4 cases of unpreventable deaths were eliminated, the mortality of this group is but 3.2 per cent. (2) Contradistinct to this, the writer presents a series of 19 cases of coma that were treated by the family physician, mostly at home, and of these 19 patients but 3 survived. This is presented with no thought of malice, but with the idea of emphasizing the importance of prompt and adequate treatment in coma.

The amount of **insulin** used in these cases varied between 61 and 685 units to bring the patient out of coma and, of course, there were many factors which entered into this, *viz.*, the duration of coma, severity of diabetes, duration of diabetes, rapidity of onset of coma, the dosage of insulin before the development of coma, and the individual reaction of the patient to insulin. John states that "coma in a child represents a major medical emergency and as such requires radical treatment, as in a surgical emergency." He feels that prompt hospitalization is necessary if the mortality rate is to be kept low, and not alone for this reason should prompt hospitalization be given, but the longer the duration of the coma, the more damage occurs to the insulogenic mechanism and the greater the amount of insulin will be required after recovery from coma.

John stresses the point that the symptomatology of diabetic coma is not sufficiently appreciated. The most common symptom is the gastric upset. These children get sick at the stomach and start to vomit and are apt to have an abdominal tenderness before drifting into unconsciousness. He feels that the gastric symptoms are due to the increased ketosis which causes digestion to cease, the acid in the stomach to increase, and the stomach to become distended. The vomitus at times is of the coffee-ground type and he feels that the degree of drowsiness in diabetic acidosis is not a good index of the patient's condition. Air hunger occasionally may be of such a degree as to give the impression of an obstruction of the larynx or an extensive pneumonia. He also stresses the point that in many of these cases the temperature is increased and there may be a leukocytosis which oftentimes gives the impression of an acute abdomen.

In regard to the treatment, John suggests putting the patient to **bed**, applying **external heat** and installing a good nurse to take care of the situation. **Adequate fluids** must be given, either subcutaneously, intravenously or by mouth. From 1½ to 4 liters (quarts) of liquid in 24 hours, depending upon the age of the child, should be given. A solution of 10 per cent **glucose** made up in **normal sodium chloride** for intravenous use and a 3 to 5 per cent glucose in saline for hypodermoclysis, 250 to 500 c.c. (½ to 1 pint) may be given every 4 to 5 hours during the day, until the patient is conscious and is able to take fluid by mouth. When this occurs, John feels that **lemonade**, **ginger ale** or **grapefruit juice** is more satisfactory than orange juice. A **Murphy drip** of normal

saline is another method of giving the fluids and this should be preceded by an **enema**. On the whole, an attempt is made to convert the metabolism into a carbohydrate one, which is done by **insulin, carbohydrate** and **saline**. If the pulse is weak or irregular, intravenous medication should be given with care. **Caffeine** or **digitalin** may be administered in these cases. If there is *nausea* and *vomiting* a **gastric lavage** is helpful as well as a **high colonic irrigation**. John feels that *small doses* of **sodium bicarbonate** are not contraindicated in diabetic acidosis but that massive doses should never be given. Occasionally, a **transfusion** may be necessary if the circulation has collapsed.

John emphasizes the point that the best treatment of diabetic coma is its *prevention* by adequate treatment, by **diet** and **insulin** and the **removal of all foci of infection**. In many of these cases there was an evidence of some temporary kidney impairment and an increase in the blood urea nitrogen.

Carbohydrate tolerance is decreased in the presence of an infection and may be combatted in one or 2 ways, *i. e.*, either by decreasing the food intake by one-third, leaving the insulin the same, or else leaving the intake the same and increasing the insulin. During infection the carbohydrate metabolism must be increased by one of these means. Whether or not the child eats makes no difference, for the metabolism goes on just the same, and insulin is required to insure the combustion of the food. He also emphasizes that the urinalysis is not always a dependable method of determining the degree of acidosis and that the  $\text{CO}_2$  should be used. He quotes Lande on the "Mechanism In Diabetic Coma," which is so concise and thorough that it is repeated here: "The breakdown of carbohydrate metabolism causes a greatly increased water excretion and an equally pronounced excretion of electrolytes normally present in the intracellular and extracellular fluids, particularly sodium and potassium. With the onset of acidosis, the excretion of ketones greatly augments the loss of water and electrolytes. As a result of the rapid loss of water, sodium and potassium, there develops a depletion of base in the body sufficient to cause dehydration of tissues, the alkali deficit becomes more marked and hyperventilation ensues with its tendency to depress blood-pressure. There develops, at the same time, an increased permeability of the capillary walls with the tendency of fluids to pass from the vessels into the tissue spaces. In mild forms the transudate is relatively free from proteins, but in severe grades of acidosis permeability is so altered that proteins pass with the fluids from the blood stream. The diminished blood volume, lowered blood-pressure, capillary stasis and escape of fluids from the blood stream combine to produce the syndrome of shock.

"During acidosis the blood is inspissated, as indicated by the normal or high serum protein and hemoglobin and the lowered blood volume. The depletion of plasma fluid is due not only to diuresis, vomiting and hyperventilation, but also to loss of fluid through the capillary walls. Recovery in part involves the restoration of serum volume, but to a certain degree serum volume and body fluid act as independent variables and the replenishment of body fluids does not necessarily result in restoration of blood volume. Circulatory failure, particularly peripheral stasis, is responsible for the escape of fluids from the circulatory system and for the failure to remain in or return to the vascular bed. Such



circulatory failure can develop when carbohydrate metabolism is proceeding in a satisfactory manner and the serum carbon dioxide is rising. In the production of coma, ketosis and alkali deficit play an indirect rôle by producing diuresis and overventilation. If shock is an important factor the restoration of the blood volume becomes an essential aim of treatment, and the blood protein figures as a measure of hemoconcentration and the blood-pressure are as important as the blood sugar and the carbon dioxide of the blood in directing treatment.

"Clinically, hemodilution seems to mark improvement. Delay in restoration of serum volume and hemoconcentration is associated with the continuance or increase of symptoms. Cases are cited in which the blood protein figures were a more accurate reflection of the clinical picture than either the blood sugar or the blood carbon dioxide. In one instance cited by Peters the patient remained in profound coma with a carbon dioxide combining power of the blood well above the critical level. The liberal administration of fluid restored consciousness without significant change in the blood carbon dioxide or the blood sugar, but with a marked decrease of blood protein."

In cases having a continued increase in temperature, blood cultures should be taken, as oftentimes they are early cases of septicemia. Occasionally, meningitis and encephalitis will be confused with diabetic acidosis, as well as trauma with concussion or a fractured skull.

**SURGERY IN DIABETES.**—There is probably no disease in which close cooperation between the internist and surgeon is of such importance as in diabetes. If this cooperation can be obtained a diabetic is no more of a surgical risk than a nondiabetic who presents the same cardiovascular and infectious state. J. T. Beardwood, Jr. (Pennsylvania M J 37:658 (May) 1934), states that the medical management of the patient with surgical diabetes readily divides itself into 4 headings, *etc.*, (1) diagnosis; (2) appraisal of the patient's general condition, (3) appraisal of the local lesion; and (4) pre- and postoperative care.

**Diagnosis.**—All patients with glycosuria are not diabetics, nor do all diabetics have glycosuria. Sugar may appear in the urine in such conditions as renal glycosuria, pregnancy, hyperthyroidism, and pituitary disease. The diagnosis in these cases is made by doing a sugar tolerance test which gives a normal curve. It is important, however, that all cases showing sugar in the urine at any time should be considered as true cases of diabetes mellitus until proved otherwise, and the diagnosis should not be definitely made of a nondiabetic condition until the patient has been observed over a period of time.

Many cases of true diabetes have a high threshold for sugar, and do not develop glycosuria even with a blood sugar twice or thrice the normal. Diabetes, therefore, should be considered in all cases presenting symptoms suggestive of, or lesions peculiar to, diabetes. Among these may be mentioned:

Gangrene of the lower extremities.

Ulcers of the feet or legs which do not heal with the usual rapidity.

Cases in which calcification of the smaller branches of the pedal arteries are visible by x-rays

Infections which do not heal in spite of adequate drainage.

Carbuncles.

Early cataracts.

Hyperthyroidism.

Though all these may be found in the absence of diabetes, they are so frequently an accompaniment that it is wise to rule out hyperglycemia as a possible etiologic factor in their existence. Do not be content with a single fasting blood sugar determination, should this be normal, but the determination should be repeated 2 or 3 hours after a meal which contains at least 50 Gm. of carbohydrate. In a nondiabetic this blood sugar reading should be normal at the end of 3 hours.

**Appraisal of General Condition.**—Such a survey can be taken properly only in those patients in whom the operation is one of election and not of emergency. *Arteriosclerosis* is the most frequent complication of diabetes. This localizes chiefly in the arteries of the lower extremities and those of the coronary circulation. Fifty per cent. of all diabetics will show a very definite disease of the coronary arteries which can be demonstrated at the necropsy table. Examinations should be directed, therefore, toward estimating the condition and degree of reserve in the cardiovascular apparatus. If possible, electrocardiograms should be made and the usual laboratory procedures done to determine the kidney function. In addition, a thorough check-up on the other systems of the body should be included. It should always be remembered that other organic disease may be present in diabetes.

**Appraisal of Local Condition**—This is limited for the most part to diseases of the lower extremities, but this is an important group and comprises the largest single subdivision of diabetic surgery. Many of these cases are preventable, and though it is not in the scope of this paper to discuss care of the feet in diabetes, it cannot be passed without emphasizing the importance of proper education and careful and frequent examinations. It is the clinician's prerogative to say when an operation should be performed, but the surgeon's, to say how and where. Unless the operator be well versed in the surgery of circulatory diseases, a careful survey by both the internist and surgeon will be of help in guiding the operator in the selection of the level of operation. Such a survey should include

- 1 Color and temperature of the foot when dependent and elevated
- 2 Palpability of the dorsalis pedis and posterior tibial pulses
- 3 Visibility of the arteries by x-rays
- 4 Oscillometric readings
5. Histamine reaction
- 6 Surface temperatures of both legs
7. Injection of lipiodol before operation

These last 4 tests are tests of refinement which may be helpful in certain doubtful cases. In the average case, however, sufficient information can be obtained with the other tests mentioned properly to evaluate the condition.

In addition, it is wise to do a Wassermann test in all cases of *gangrene*, as the presence of syphilis will frequently influence the prognosis and treatment. The presence of syphilis frequently can be anticipated by the appearance of the

extremities Should *syphilis* be present, it should be actively treated with **mercury** and **iodides**.

**Pre- and Postoperative Treatment.**—This heading naturally divides itself into 2 subheadings, *viz.*, the care of patients having operations of election and the care of those having operations of emergency.

In the cases of *operation of election*, it is wise to admit the patient to the hospital 5 to 10 days before the operation unless he has been satisfactorily standardized at home. It is the writers' custom to place these patients on the same maintenance **diet** as would be done in the case of patients who were admitted solely for the standardization of the diabetes. It is important that whatever formula is chosen for calculating the diet, the carbohydrate portion be relatively high and the fat portion relatively low, if the danger is to be avoided of the development of acidosis from the diet alone. A formula that has been found satisfactory in these cases is based on the ideal or expected weight of the individual according to sex, height, and age. An allowance is made of 2 Gm. ( $\frac{1}{2}$  dram) of carbohydrate, 1 Gm. (15 grains) of protein, and 2 Gm ( $\frac{1}{2}$  dram) of fat per kg. ( $2\frac{1}{8}$  lbs.) of ideal body weight per day. This has a caloric value of 30 calories per kilogram. The diet should be individualized for each patient, but in preoperative preparation it is seldom necessary to give more than 2100 calories.

The patient is placed on this diet, a blood sugar determination made each morning, a plasma, carbon dioxide, a blood urea-nitrogen determination made on admission, and a 24-hour specimen of urine examined for sugar, acetone, and diacetic acid. If after 48 hours the blood sugar is still considerably above normal, **insulin** is indicated. It is impossible accurately to foretell the dosage of insulin that will be required in any given case. A method is to subtract 100 from the blood sugar value expressed in milligrams per 100 c.c. and divide by 5 (the blood sugar determination chosen should be approximately the average of the determinations over several days). If more than 15 units are required, it is wiser to give 2 doses, if more than 30 units, 3 doses. It should be emphasized that this is only a rough estimate for determining the initial dose, and it must be increased or decreased, depending upon the subsequent laboratory findings.

It is important to bear in mind the complicating coronary sclerosis and not to attempt to depress the level of the blood sugar too low. The level which the writer has adopted as the most satisfactory and safe one is the patient's age plus 100, expressed in milligrams per 100 c.c. Thus, in a patient aged 50, no attempt would be made before or after operation to get the blood sugar below 150 mg. Even in children, it is inadvisable to get the level too low, as it means that these patients have less of a glycogen reserve to call upon during and immediately after operation. If the blood sugar has reached a satisfactory level, and there is no evidence of acidosis as revealed by the laboratory examination, these patients are then ready for surgical procedure. It should always be the prerogative of the medical man to say when these patients should be operated on.

Once the patients have been standardized, it is important to carry them through the *postoperative period* on the same total **glucose** and **insulin** that they received before operation. The total glucose of the diet may be calculated

according to the formula of Shafer and Woodyatt—total glucose equals 100 per cent. carbohydrate plus 10 per cent of the fat plus 60 per cent. of the protein. The amount of glucose is divided into 4 equal doses, as is the insulin, and one-fourth the total glucose is given 3 hours preoperatively. Unless there is some contraindication, this may be given by mouth as orange juice, ginger ale, or oatmeal gruel, to which glucose has been added to make up the total carbohydrate content. If given much nearer the operation than 3 hours, the stomach frequently retains it because of pylorospasm and it may be regurgitated later. A blood sugar and plasma carbon dioxide determination is done 3 hours after operation and the insulin dosage adjusted if necessary, the remaining glucose being given at 6-hour intervals during the 24 hours. This may be given by mouth if the patient's condition permits, or it may be given by vein. A method that has been found satisfactory is to administer it through a Jutte tube which is passed through the nose and into the duodenum. This has the advantage of resting the stomach, and it may be unnecessary to remove the tube for 48 hours. As the patient's condition improves, it will be possible to restore his diet, first as a semiliquid or soft diet, and then as a full diet, and the insulin may be allocated accordingly. It is important not to allow the blood sugar to reach too low a level and hyperglycemia should be avoided at all times, if possible.

In cases of *emergency operation*, which are largely confined to acute abdominal conditions, it is important to remember that diabetic acidosis frequently will give all the symptoms of an acute condition within the abdomen such as nausea, vomiting, abdominal pain and tenderness, increased temperature and leukocytosis. During the past year, the writer has seen 4 patients who were referred to the hospital with the diagnosis of an acute condition within the abdomen but which were actually cases of diabetic acidosis.

Acute conditions within the abdomen may occur in the diabetic and require the same prompt and thorough treatment as in the nondiabetic. It is wise, however, to do the usual laboratory studies for a diabetic who presents symptoms of nausea and vomiting, in order to rule out acidosis. These can usually be done in 30 or 40 minutes, and there are few cases of such emergency that this slight delay will be of serious consequence in the ultimate outcome of the surgical condition, and it may be the means of preventing a useless laparotomy.

It is the writer's custom in all emergency operations to administer immediately before operation 30 to 40 Gm. (1 to 1½ ounces) of **glucose** intravenously with a dosage of **insulin** which is dependent somewhat upon the laboratory findings. This supplies nourishment for the myocardium and at the same time gives a certain amount of glucose which prevents the development of acidosis and carries the patient through the postoperative period. No attempt should be made to depress the blood sugar too low, either before or after operation, and these patients may be carried along on frequent small doses of insulin until they can be placed on a maintenance diet. The management of these cases from this point does not vary from that of the operations of election.

In the presence of *acidosis* and *coma*, it is wise to postpone any surgical procedure until the acidosis can be controlled. From 30 to 50 units of **insulin**, depending upon the height of the blood sugar, should be given immediately. In

addition, a **high compound enema** should be given, and a **gastric lavage** should be done if there is any vomiting. The patient should be put in a **warm bed** and **external heat** applied; 30 Gm. of **glucose** should be administered every 2 or 3 hours, balanced with an appropriate dose of **insulin**. It is wise also to **force fluids**, either by vein, subcutaneously, or by mouth. Sodium bicarbonate or alkalis in any form are contraindicated in diabetic acidosis.

An analysis of the writer's cases shows that almost one-third had gangrene. The number of *goiters* (2) is much less than would be anticipated from the figures of Joslin and Lahey. According to their statistics, 3.85 per cent of patients with diabetes have *hyperthyroidism*. It is interesting to note that there were 6 cases of *pregnancy*—this is a problem which will be of greater significance in the future. In 11 cases the diabetes was not discovered before operation and of these 5 died and 2 developed severe infections. It is noteworthy that in the past 2 years there was no case in which diabetes was not discovered before operation. The question of *syphilis* has been briefly discussed. It apparently did not influence the mortality rate, and, indeed, renders the prognosis of cases of gangrene a trifle more favorable.

**OBESITY.—Treatment.—Dinitro Compounds** \*—The literature on obesity for the year 1934 is, for the most part, taken up with a discussion of dinitrophenol and the other dinitro compounds in the treatment of this condition. There are many enthusiasts of this method of treatment and also many clinicians who consider that these preparations should never be used because of their occasional toxic effect. Solomon Silver (*J A M A* 103:1058 (Oct 6) 1934) reports a case of agranulocytosis occurring in a patient taking dinitrophenol. According to the history which he obtained, the amount of drug taken was well within the recognized dosage limits, and while he states that no causal relationship can be established between the use of the drug and the patient's death, he feels that this should be regarded as a possibility. A. M. Hoffman, E. M. Butt and N. G. Hickey (*Ibid* 102:1213 (Apr 14) 1934), in reporting cases of agranulocytosis following the use of amidopyrine, also report a case in which dinitrophenol was taken.

Henry Dintenfuss (*Ibid* 102:838 (Mar 17) 1934) reports a case of dinitrophenol intoxication in which after 4 days' treatment the patient complained of severe exhaustion which was accompanied by a rash over the chest, extreme dizziness and a sensation of fullness in both ears. Discontinuing the drug, the symptomatology very gradually disappeared but returned again, when it was taken for a day or so, a month later. Following this dosage, the otalgia and impairment of hearing persisted and when the patient was examined by the writer, he found that both drumheads were reddened and bulged. There was an obliteration of the landmarks on both sides and a definite diminution in hearing, which he states was of a catarrhal nature. Seven months after discontinuing the dinitrophenol, the aural inflammation subsided, but the impairment in hearing persists.

\* See also Section on THERAPEUTICS, GENERAL DINITROPHENOL  
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Observations in 2 cases convinced A. de Chatel and J. Motika (Orvosi hetil. 78:831 (Sept. 8) 1934; Deutsche Arch. f. klin. med. 176 700, 1934) that alphas-dinitrophenol is not a harmless drug, for even if given in therapeutic doses, it produced symptoms that indicate an impairment of the kidneys and of the myocardium. The cardiac disturbances were demonstrated in electrocardiographic tests on the patients and they were corroborated in experiments on cats. Moreover, dinitrophenol does not always accomplish its aim, for in one of the patients the highest therapeutic doses changed neither the metabolism nor the body weight, and in the other case the weight did not increase much until the sense of taste had become impaired and the patient had lost her appetite.

E. N. Davidson and M. Shapiro (J. A. M. A. 103:480 (Aug. 18) 1934) report a case of *agranulocytic angina* following dinitrophenol. The patient was taking 300 mg (5 grams) a day and after 2 weeks of this dosage, developed aggressive pain and swelling of the gums and submaxillary glands. She also had a chill and increase in temperature which reached 103° F. (39.4° C). Before admission she had noticed a yellowish tinge of the scleræ and this was present upon admission. This patient recovered following use of **pentnucleotide** and **leukocyte cream**.

Possibly the most sensible summary is that of E. L. Bortz, Anthony Sindoni, Jr., and E. M. Hobson (Pennsylvania M. J. 38 170 (Dec.) 1934). They report their experiences in the metabolic clinic of the Lankenau Hospital as follows:

"Dinitrophenol is but one of a whole series of those interesting chemicals, the dinitro compounds, that is now undergoing investigation. The following table has been compiled from the findings of Heymans and his associates, using dinitrophenol as the unit of comparison:

	Relative Activity	Toxicity	Azoreaction
Dinitroaminophenol	16.4		
Dinitronaphthol	99.3	+++	
Dinitrophenol	100.0	+++	
Dinitrothymol	178.2	++	-
Dinitrohexylphenol	395.1		+
Dinitrocresol	207.5	++	?
Dinitropentylphenol	455.5	+	++

"Although dinitrophenol is both slightly more active and slightly more toxic, dinitrophenol and dinitronaphthol are considered approximately in the same category. Dinitrophenol, the most widely used of the compounds, is believed to be the most toxic. Dinitrocresol, dinitrothymol, and dinitropentylphenol are said to be more active with a much lower toxicity. Heymans found that dinitropentylphenol is the most active of the series and does not possess the general toxic properties evidenced by the others, especially dinitrophenol; therefore, the stimulating action of dinitropentylphenol on cellular metabolism must be not only the most intense, but also the most specific.

"Heymans and his coworkers believe that the intensity of action of the different preparations depends upon the rapidity with which aromatic amines

are formed and that this is evidenced by the appearance of a positive azo-reaction. The table above shows the relative activity of the different compounds.

"A series of experiments with dinitropentylphenol conducted in the same laboratory indicated that acetaldehyde, one of the intermediary products of the reaction, diverts the cellular action of the drug and that the effect of fatal doses can be inhibited by the intravenous injection of sufficiently large doses of glutathione or acetaldehyde, either preventively or curatively.

"Earlier experiments had shown that the dinitro compounds cause a notable accumulation of lactic acid.

"From the various findings, the authors concluded that these chemicals have 2 different actions: (1) A direct accelerating action on the cellular ferments which take place in an alkaline medium and is probably exercised through the sulphydral system; (2) a combustion of the intermediary products (particularly acetaldehyde and probably methylglyoxal), especially produced in an acid medium.

"It is not unlikely that the above preparations are forerunners of compounds which will prove to be of great value in the hands of the medical profession when the problems of metabolic stimulation arise.

*"Limitation of Diet and Use of Sodium Dinitrophenol*—Sodium dinitrophenol as a metabolic stimulant is now being used in the obesity clinic of the Lankenau Hospital to replace diet for reducing body weight, but is proving to be a great asset as a means of encouraging the consistent adhering to a diet moderately low in calories over a long period of time. For example, patients requiring approximately 1800 calories of food daily, can lose  $2\frac{3}{4}$  lbs. of weight per week by following a 1200 calorie diet and taking 3 capsules of 100 mg ( $1\frac{1}{2}$  grains) each of dinitrophenol daily, although on the same diet without the dinitrophenol only  $\frac{1}{2}$  to 1 pound is lost weekly. A patient wishing to lose 60 or 80 pounds of excess weight soon loses enthusiasm and becomes discouraged if progress is not more apparent.

"Patients who have lost 20 to 30 pounds of weight by limiting their daily caloric intake to 1200 calories for a period of 1 or 2 years learn to satisfy their appetite and to be contented with the prescribed diet, but they will soon lose interest when the customary treatment will no longer cause a loss of body weight. A more rigid restriction of foods would not be advisable, as it frequently causes a lack of cooperation, and a break in the dietary régime will renew the patient's interest in food. By taking dinitrophenol and continuing their accustomed diets, patients are able to lose 10 to 15 pounds without becoming antagonistic toward diet therapy.

"After being on a diet moderately limited in calories for 1 or 2 years, the plastic individual has established new food habits. He has learned to prefer large quantities of the crisp and watery 5 per cent. vegetables such as string beans, cucumbers, cauliflower, asparagus, and tomatoes to the dry, starchy 15 and 20 per cent. vegetables such as peas, corn, lima beans, and potatoes. He has learned to enjoy fresh unsweetened fruits, and does not desire large amounts of concentrated foods such as bread, cereals, butter, candy and ice cream.

"Many of the prescribed diets that are low in calories and limited in choice of foods, such as the skimmed milk and banana diet which is popular at the present time, or the well-known lamb chop and pineapple diet, as used a few years ago, are so far removed from the normal meal that the patient cannot enjoy the family bill of fare nor learn to select foods in an intelligent manner. After a desired amount of weight has been lost, as it will be on these unbalanced diets, the person will resume the faulty food habits through which he gained the unwanted weight, for he has not had the opportunity to adjust himself to correct food habits which will enable him to maintain a normal body weight

"For the past 2 years, clinical investigations have been carried on in the Metabolic Department of the Lankenau Hospital in an endeavor to determine the clinical value, indications, contraindications, and limits of safety of the dinitro compounds, and the basis of this paper is a study of their action in a group of 60 obese patients.

"These individuals ranged in weight from 150 to 400 pounds and were under treatment for a period of time varying from 2 weeks to 10 months. Twelve of the series (20 per cent) were males and 48 (80 per cent) were females. The average weight loss while taking dinitrophenol was between 2 and 3 lbs. per week, whereas on diet alone from  $\frac{1}{4}$  to 1 lb. weekly was lost. The majority of the patients liked the treatment and were satisfied with the result obtained. The frequent untoward effects, however, were such that the value of dinitrophenol as a metabolic accelerant is limited.

Toxic Symptom	Cases	Per Cent
Pruritus	12	20
Urticaria	18	30
Edema	4	7
Nausea and vomiting	7	12
Diarrhea	3	5
Jaundiced appearance	2	3
Elevation of blood-pressure	1	2
Hyperpyrexia	4	7
Nervousness	4	7
Headache	4	7
Loss of taste	2	3
Numbness of extremities	2	3

"The quantity of dinitrophenol necessary to produce loss of weight in patients who are on a generous unrestricted diet is so large in the majority of cases that the factor of safety is practically eliminated. For this reason it is wise to use the drug only as an adjunct to moderate limitations in diet. Comparing the weight loss on a measured restricted diet without dinitrophenol to a similar program using dinitrophenol, the interval of time required for reduction is cut approximately one-half.

"Various modifications in the method of administration have been tried but the accepted one is to give 1 capsule of 100 mg. ( $1\frac{1}{2}$  grains) after the largest meal of the day for 1 week. If this is well tolerated, the dose may be raised to 2 capsules daily for a week, and to 3 capsules daily in the third week, which



schedule is to be followed for as long a period as is deemed wise. Although larger doses have been given, it is not recommended.

"Patients may show symptoms of intoxication after a very few doses have been ingested, or they may appear tolerant to the drug for several weeks and then suddenly develop toxic symptoms. Patients who showed an optimum response therapeutically over a period of several weeks, exhibited toxic symptoms in 3 cases when the dose was slightly increased.

"Thus far no known method exists to determine the susceptibility to dinitrophenol except that of trial and error, *i. e.*, by the use of small doses of the drug. Our clinical impression is that patients with an allergic background more frequently exhibit symptoms of hypersensitivity than those with a negative allergic history. In several of the present series, if symptoms of toxicity appeared, the drug was promptly withdrawn but after an interval of 10 days was again administered, beginning with 1 capsule daily. Larger doses were tolerated than before the toxic reaction, and weight loss was satisfactory.

"The use of dinitrophenol in winter is complicated by the increased susceptibility of subjects to respiratory infections while perspiring. In many cases the use of the drug during the summer coincides with periods of hypersensitivity to foods, pollens, and dust, and the drug aggravates the symptoms. The use of this preparation, therefore, is more satisfactory in the spring and autumn. When symptoms of intoxication appear, the drug is promptly stopped, the diet is increased, and the patient is given alkalis.

"Patients with the exogenous type of obesity respond much more readily to dinitrophenol than those with the endogenous or glandular type. The drug is a substitute for thyroid extract only in so far as augmentation in metabolism is produced. The symptoms of thyroid dysfunction due to sympathetic nervous system involvement, which respond to thyroid extract medication, are not influenced by dinitrophenol administration.

"All of the patients in the present series experienced a sensation of warmth, and as dosage was increased the majority perspired profusely, but less so in the winter than in the summer. The drug produces a fever in practically all cases as the dosage is raised, but in none of this series was the febrile reaction over  $102^{\circ}$  F ( $38.9^{\circ}$  C) and in most it never exceeded  $100^{\circ}$  F ( $37.8^{\circ}$  C).

"With small or moderate quantities of the drug the basal metabolism did not vary greatly, but as the dosage was increased the metabolic rate could be elevated as much as 50 per cent. Accidents and untoward effects are less liable to occur when the basal rate does not exceed plus 20.

"With the chemical characteristics and physiologic reactions of the newer dinitro compounds better defined, the use of the drugs for clinical experimentation will naturally follow. The action of dinitrocresol has been studied in 1 patient in the present series of cases. The patient was on a measured diet and had previously taken dinitrophenol for a period of 5 months with no ill effect and with a loss of 90 lbs. in weight. He was given 1 capsule daily (50 mg —  $\frac{3}{4}$  grain) of dinitrocresol in the form of dekrysil for 8 days. On the seventh day, however, the patient developed jaundice and complained of pain in the right upper quadrant of the abdomen. The icteric index was 12.6. It was necessary to discon-

tinue the drug because of the apparent hepatic toxicity, but weight loss continued without medication. Further experiments will be reported later."

An impartial evaluation of many controversial papers is convincing of the fact that dinitrophenol is a useful metabolic stimulant which possesses definite toxic reactions in a certain number of patients. It is a drug in which the margin of safety between an adequate dose and a toxic dose is very small. It is a substance which has a very definite use in the field of obesity and weight reduction, but with the present knowledge of its action it should be used with care and only in cases in which the metabolic appraisal has been made, and when it is used, patients must appreciate the importance of reporting at frequent and regular intervals, so that any early untoward effects may be noted and the drug discontinued. No doubt, further work with these preparations will more adequately acquaint the clinician with their field of usefulness and will result in a safer dosage and method of administration, but it behooves the physician to emphasize to his patients the danger of the indiscriminate use of these preparations.

# **Diseases of Respiratory Tract**

*by*

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**BRONCHI.**—*Diagnosis.*—R. A. Bendove, and B. S. Gershwin (Am. J. Roentgenol. 31: 323 (Mar.) 1934) state that when iodized oil is injected intratracheally, it tends to delineate the bronchi and alveoli in an inverse proportion, *i. e.*, the more the alveoli are outlined, the less the bronchi are visible, and *vice versa*. This inverse ratio in the visibility of the iodized bronchi and alveoli is of diagnostic significance. In a normal lung the outlined alveolar element predominates, overshadowing all the bronchi, and the x-ray image simulates a tree in midsummer. Diseased and dilated bronchi retain most of the injected material, and few, if any, of the alveoli in the corresponding territory will be delineated in the x-ray picture. In cases of extreme cylindric dilatation, the filled bronchi resemble the branches of a tree in winter, with no remnant of the former foliage. The absence of the alveolar leaves may be general or localized, depending on the extent of the bronchial dilatations. Any bronchus that retains the iodized oil 15 minutes after its injection is to be considered functionally impaired, irrespective of its morphologic appearance. In order to maintain definite standards of comparison, it is advisable always to inject 20 c.c (5 drams) of the iodized oil and to outline only one lobe at a time.

**BRONCHIECTASIS.**—*Diagnosis.*—In a study of bronchiectasis by W. P. Warner and D. Graham (Arch. Int. Med. 52: 888 (Dec.) 1933), particularly in reference to triangular basal shadows, they endeavored to determine the significance and cause of the shadows and have produced them experimentally. It was found that triangular basal shadows as seen in x-ray pictures of the chest are diagnostic of bronchiectasis. Their presence should always be taken as an indication for the injection of iodized oil to confirm this diagnosis. They occurred in about 6 per cent of all cases of bronchiectasis. Triangular basal shadows are caused, in some cases at least, and probably in all cases initially by a lobar atelectasis of the bronchiectatic lobe. It is believed that the cause of this lobar atelectasis is the plugging of the terminal bronchioles by the swelling of the bronchial wall with an inflammatory exudate. Lobar atelectasis produced in dogs by completely occluding the bronchi of the lower lobes caused typical triangular shadows due to the atelectatic lower lobe. Atelectatic bronchiectatic lobes may occasionally be found on physical examination, such physical signs are diagnostic of bronchiectasis. Bronchiectasis may occur in the absence of both fibrosis of the pulmonary parenchyma and pleural adhesions.

W. E. Anspach (Am. J. Dis. Child. 47: 1011 (May) 1934) draws the following conclusions from necropsies and x-ray and clinical study of the atelectatic bronchiectatic process of the lower lobe in 50 cases in children. The study lasted throughout life in some and from infancy to puberty in others. (1) The small, well-defined triangular shadow with associated displacement of surrounding structures toward it, frequently noted at the base of the lung in x-ray pictures of children, represents a lower lobe in various degrees of collapse. (2) While anomalous lobes are frequently seen at necropsy, persistent consolidation or collapse of a supernumerary lobe in the region of the cardiohepatic angle is rare. The smallest shadows were found to represent a regular lower lobe. (3) Necropsies of infants in whom the triangular shadow was present during life did

not show dilated bronchi, but in children who continued to live, changes in the triangular shadow appeared later, and bronchiectasis developed. (4) If air entered the collapsed lobe early, the triangular shadow fluctuated in size and was larger and less dense in proportion to the amount of inflation. If postural drainage was instituted early, these fluctuating triangular densities, even though present for years, did not always bring about bronchial dilatations. The triangular shadow is not "pathognomonic of bronchiectasis." (5) If the triangular shadow fails to fluctuate, bronchial dilatations may develop within a few months, but frequently the process covers a period of years. (6) These triangular patterns, when outlined by opaque oils, are frequently seen in adults with bronchiectasis and appear to be acquired rather than congenital. (7) The prognosis may be more accurately determined by observing the behavior of these shadows at successive x-ray examinations. (8) Atelectasis precedes and plays a prominent and most constant part in the development of a common form of bronchiectasis of the lower lobe. (9) The most common form of bronchiectasis in children is an acquired process. (10) Early and frequent drainage of the bronchi is essential if the development of bronchiectasis is to be avoided.

**Treatment.**—*Pneumonectomy*.—E. Windsberg (Rhode Island Med J 17: 163 (Oct) 1934) reports one of the 6 cases of successful pneumonectomy, a case of bronchiectasis of 5½ years' duration in a girl of 12 years, involving the right lung, whereas the other five involved the left lung. When bronchiectasis, not amenable to postural drainage and bronchoscopic therapy, is confined to one lobe of a lung, lobectomy offers a reasonably good prospect for a complete cure. The method of Graham not only establishes drainage but also destroys diseased lung tissue in multiple stages. In the author's case the method of Graham was employed to begin with because of the multiple cavities and the extensive involvement. Amputation at the hilus was effected at the fourth sitting, when it appeared relatively safe. On the other hand, pneumonectomy as a primary procedure would have been hazardous in this case. The wound in the wall of the chest has healed completely except for the opening of a small bronchial fistula high up in the axilla, the size of a pinhead. The fistula has closed, only to open again, on several occasions. Injection of iodized oil shows it to be about 1½ inches in length and to lead directly to the stump of the main bronchus. It is felt that a partial thoracoplasty may be required to effect permanent closure of the fistula as well as to overcome the extreme deviation of the trachea to the right. During the past year the patient has gained in weight and in height. She has carried on well under unfavorable home conditions. Moderate dyspnea develops only following considerable exertion. Cough and expectoration are insignificant and are due entirely to the presence of the bronchial fistula. Since September, 1933, she has been attending school for the first time in her life.

**LUNGS.—ABSCESS.**—*Treatment*.—E. Sergent and R. Kourilsky (Arch Méd-chir de l'app respir 9 49, 1934) performed 25 operations on the phrenic nerve in bronchopulmonary suppurations—**phrenicectomy** in 23 cases and **alcoholization** of the nerve in 2 cases. From the results, phrenicectomy is

absolutely contraindicated in cases of putrid abscesses with inflammation, particularly if the abscesses are on the left side in either the upper or lower lobe. In cases of putrid abscesses that are not very active, particularly those in which the abscesses are in the right middle lobe, phrenicectomy may bring about remissions not exceeding 3 months in duration. It cannot be considered a truly curative method for putrid abscess. It is generally ineffective and it may be dangerous. There is risk of allowing the most favorable time for surgical operation to pass. Phrenicectomy in cases of abscess is more apt to hasten the course of the disease than to effect a cure, as it seems to activate acute inflammatory processes

Its mode of action is not very clear, but a comparison of its immediate effects with those of limited thoracoplasty shows a curious resemblance, as both procedures are followed by temporary arrest of the expectoration and a tendency toward diffusion of the inflammation. It is probable, therefore, that both operations have a mechanical effect consisting in partial immobilization of a portion of the side of the thorax operated upon and compression of the adjacent lung

It was found that in cases of isolated cylindrical bronchiectasis of the left lower lobe, phrenicectomy may bring about *temporary* improvement only.

**ATELECTASIS.—X-ray Diagnosis.**—C. M. Van Allen, W. A. La Field, and P. S. Ross (Radiology 22: 27 (Jan.) 1934) report that because of the disagreement with regard to the definition of atelectasis and the absence of pathognomonic signs, the x-ray diagnosis of the condition has not been entirely satisfactory

Atelectasis is defined as a totally airless state of either a part or all of the lung, with collapse of the small airways and alveoli. This definition applies to the three recognized types of the condition, *i e*, the congenital, the obstructive, and the compressive

Recently the term "atelectasis" has been used to include various states in which the pulmonary tissues are partially air-containing, the collapse not being complete, or in which the alveoli are filled with exudate and are not collapsed

Pneumonia and atelectasis should not be confused, although areas of atelectasis may develop in the course of pneumonia when bronchi become plugged by the viscid exudate. Pneumonia is more prone to develop in areas of obstructive atelectasis that are contaminated with pneumococci than in a similar normally aerated lung

Areas of hypoventilated lung should not be classified as atelectasis as they carry on a definite, though decreased, respiratory exchange, while atelectatic tissues are wholly without external respiration

The characteristic x-ray signs of atelectasis are produced by the reduction in size of the affected tissue. The diaphragm on the affected side is elevated and part or all of the mediastinum is displaced toward the involved side. At times, the intercostal spaces on the atelectatic side are narrowed, while those on the other side are widened. The spine may show scoliosis with the concavity toward the lesion. During respiration the affected side moves less, and the opposite side more, than normally, as evidenced by the excursions of the ribs and dia-

phragm The mediastinum moves toward the side of the lesion on inspiration and away from it on expiration.

Bilaterally symmetrical atelectasis produces none of the displacements described.

These x-ray features of atelectasis are quite generally agreed upon, but there is considerable variation in the interpretation of the shadow cast by the pulmonary tissues themselves The lung shadows have been variously described as homogeneous, mottled, streaked, slightly hazy, and extremely opaque, but no one has made use of these variations to differentiate the types of atelectasis or to distinguish atelectasis from other conditions producing increased density of the lung.

All of these signs have been found in other pulmonary diseases Diaphragmatic elevation occurs in 55 per cent. and mediastinal displacement in 12 per cent. of cases of pneumonia Fibroid pulmonary tuberculosis produces findings similar to those in obstructive atelectasis.

The authors determined to search for a means of more accurate diagnosis between atelectasis and other lesions causing pulmonary consolidation.

The term "atelectasis" was used to denote complete airlessness and alveolar collapse, massive or focal.

X-ray pictures of excised dog lungs in which atelectasis had been produced by obstructing a bronchus were made first and compared with those of the same lungs after they had been artificially reinflated Next, x-rays of fresh atelectatic human lungs of all types obtained at autopsy were made, studied, and checked by histological examination Then, x-rays of the chests of living human subjects presenting these lesions, determined by careful clinical observation, were made The lung shadows of the 3 groups were studied and compared as to composition

It was found that the lung shadow was completely homogeneous only when the lung tissue was entirely free from air Even an extremely small amount of air, detectable only by microscopy, is plainly revealed by the x-rays

A completely airless lung consistently gives a homogeneous "ground-glass" shadow if (1) the dosage of x-rays is sufficient to penetrate the tissues and demonstrate their radioconsistency, and (2) the shadow of the lesion is large enough to permit discernment of its consistency.

The other common consolidations of the lung which are confused with atelectasis cast a definitely heterogeneous shadow because of the presence of residual air While a few other lesions present the ground-glass shadow of complete airlessness, these can usually be distinguished readily by other signs

The relative sizes of affected lobes is of importance Measurements show that a completely atelectatic lobe is very much smaller than normal during both inspiration and expiration In pneumonia the affected lobe is of about normal size during expiration but much smaller than normal during inspiration There is a high position of the diaphragm on the side of a pneumonic lesion during inspiration but never on expiration, while in atelectasis the diaphragm is high during both phases of respiration.



The ground-glass shadow is constant in atelectasis unless shadows of irregular density are superimposed upon it. In massive atelectasis the area of even density is easily seen. In focal atelectasis the areas may be so small as to be obscured, but the characteristic evidences of visceral displacement are constant.

In pneumonia, the x-ray shadow of the lung is always heterogeneous because of the presence of air, and visceral displacements due to reduction in the size of the lung are absent or limited to the inspiratory phase.

A tuberculous lung also gives a heterogeneous shadow except in caseous areas, which are usually small. Small scattered tuberculous lesions may be difficult to differentiate from focal atelectasis, especially if visceral displacements occur at both inspiration and expiration, as may be the case in fibrous tuberculosis. Under such conditions focal atelectasis can usually be ruled out as it rarely occurs so chronically as tuberculosis. If the lung is compressed by pneumothorax it may be impossible to distinguish focal atelectasis from tuberculosis.

Hemorrhagic infarcts produce a mottled shadow, although they may cause visceral displacements after fibrous shrinkage.

Pulmonary hypoventilation can be distinguished from atelectasis by absence of the ground-glass shadow.

An extrapulmonary mass encroaching upon the lung field produces a ground-glass shadow unless lung tissue overlays it, but the visceral displacements are usually not characteristic.

When massive atelectasis and another consolidative lesion occur in the same part of a lung the ground-glass shadow of the atelectasis obscures the other lesion unless calcified areas or air-containing cavities are present.

In neoplasms of the lung associated with obstructive or compressive atelectasis the shadows of the two lesions are indistinguishable. In the obstructive type visceral displacements may be present, but in the compressive type they are absent.

**EMBOLISM. — *Diagnosis.*** — In discussing the differentiation of acute coronary artery thrombosis from pulmonary embolization, S. H. Averbuck (Am J M Sc 187. 391 (Mar) 1934) states that the clinical picture of an acute coronary artery thrombosis is difficult to present briefly. The symptoms and signs depend upon the artery involved, the state of the other cardiac arteries and myocardium, and the reaction of the individual affected. Nevertheless, there are certain features which occur commonly. Severe substernal, epigastric or precordial pain which appears suddenly perhaps radiating to the left or right shoulder, to the neck or to the jaw, is frequent. Dyspnea need not be a pronounced symptom; it may be present in moderate degree. In the hyposensitive or in isolated left ventricular failure due to closure of a medium-sized artery dyspnea may be severe. Often the breathing is shallow, rapid and restrained. With occlusion of a larger coronary vessel, cyanosis may be slight, patients presenting rather an ashen-gray color. Sweating, coldness of the extremities, a rapid, thready pulse, diminished blood-pressure, and feeble heart sounds complete the general picture of shock. Sudden death is common. Pericardial friction rubs, basal lung râles or pulmonary edema occur.

Pulmonary embolus usually induces a syndrome characterized by the sudden appearance of painful oppression somewhere in the chest, *with extreme cyanosis and dyspnea*. The pain has no typical radiation and often may be described as a strangling sensation, a sense of intrathoracic suffocation which provokes an *angor animi* as profound as that which occurs in angina pectoris or coronary thrombosis. In many cases shock accompanies the onset, and death occurs almost immediately. In those cases which survive the original shock, dyspnea and cyanosis, fever, and the appearance of pulmonary râles and abnormal breathing constitute the clinical picture. In other cases the heart fails comparatively rapidly. Increasing cyanosis, quickly enlarging liver, and dilatation of the heart to the right signify the right ventricular failure. Cough with the expectoration of sanguineous sputum, pleural rubs and painful respiration depend upon the branch of the pulmonary artery and the area of lung involved. Recovery is not uncommon.

Thus, it is obvious how confusion in the diagnosis of these two syndromes might readily result. Accurate diagnosis becomes even more difficult in the frequent atypical forms. Hyposensitive individuals may suffer a coronary artery closure without pain, but experience severe dyspnea instead, while pulmonary emboli may cause severe pain in the left side of the chest, or occur without hemoptysis. Such cases, as well as those with little cyanosis and dyspnea, because of rapidly ensuing shock, present the most difficult problems in differential diagnosis.

When the clinical picture suggesting coronary artery thrombosis occurs in a female patient who has neither arterial hypertension nor diabetes, a pulmonary embolus should be suspected. The high incidence of embolic phenomena in the female sex arising from abnormal pelvic conditions is an important factor in this condition. If the history or physical examination brings to light existent or previous evidence of peripheral vascular involvement, *i. e.*, phlebitis, unilateral leg edema, pelvic disease or lower extremity abnormalities, the likelihood of the coronary syndrome being caused by an embolus to the lungs is strengthened.

Occurring postoperatively, the clinical picture of pulmonary embolus simulates coronary thrombosis. When it is recalled that pulmonary emboli are very frequent after operation and that coronary artery thrombosis is comparatively rare because patients with coronary artery disease are spared any but emergency surgical procedures, such cases will be correctly analyzed. A diagnosis of coronary thrombosis should only cautiously be made in a patient presenting the syndrome under consideration who does not give a history suggesting coronary artery disease, *i. e.*, anginal attacks, "gastric" symptoms, etc. Pulmonary embolism may explain the syndrome in such an instance.

In a hyposensitive individual, when the diagnosis of coronary artery thrombosis is made in the absence of pain, and dyspnea is an outstanding sign, the possibility of a pulmonary embolus must be excluded. Severe dyspnea and marked cyanosis, even in the presence of pain, should direct attention to this diagnosis, for these signs are the most striking and characteristic of pulmonary embolus. The dyspnea is severe, taking the form of rapid stertorous breathing, signifying a genuine air hunger. The cyanosis is usually very marked and generally exceeds

that of coronary artery thrombosis. Unfortunately, the location and radiation of the pain in coronary artery thrombosis are so variable that from these features alone, in any given case, differentiation cannot be made from the intrathoracic pain induced by a pulmonary embolus.

The conditions may coexist. Coronary artery occlusion with resulting myomalacia cordis is not infrequently the cause of ventricular mural thrombosis. As the left anterior descending branch of the left coronary artery is the one most commonly involved, and, according to Gross, supplies small parts of the right ventricle and the septum, right ventricular mural thrombosis may occur after left coronary artery occlusion. Therefore, pulmonary emboli may readily complicate this condition. When both conditions are present, the association outlined above does not necessarily hold. In 2 cases of this association, the origin was not intracardiac, but in the lower extremities. However, wherever the emboli arise, the symptoms caused by a pulmonary embolus in a patient who has proved coronary disease may so simulate a coronary occlusion as to be impossible of differentiation. Unless the manifestations of the embolus are typical, with right side chest pain, pleural rubs and hemoptysis, the condition goes unrecognized, to be disclosed only in the pathologic study. Differentiation in this kind of case is perhaps of pure academic interest and it suffices here merely to point out the problem involved.

X-ray films of the lung always serve as an important means of determining the presence of pulmonary lesions. Unfortunately, the gravity of the general condition of these patients usually contraindicates this procedure.

J. P. Anderson (Bull. Am Heart A 3 5, 1933) investigated the electrocardiographic findings in experimentally induced embolism in dogs. He found fairly consistent changes, such as "tachycardia with disturbance of S-T segments with inverted T waves. Coronary T waves were encountered only once. The work suggests a rather more rigid requirement for the electrocardiographic diagnosis of coronary thrombosis, but whether the tracings are sufficiently differentiated to warrant electrocardiographic diagnoses of pulmonary embolism is uncertain." Similar studies should be repeated on man in order to establish the electrocardiographic changes in pulmonary embolism. Pathologic studies must also be taken in order to correlate the artery and lung involvement with the electrocardiographic findings.

**Treatment.**—Aside from the desirability of diagnosing disease as accurately as possible, the differentiation of pulmonary embolization from coronary thrombosis has a practical aspect. Pulmonary emboli have been successfully removed surgically by M. Kirschner (Arch f klin Chir 133:312, 1924) and by A. W. Meyer (Surg Gynec Obst 50 891 (May) 1930) who used the method first described by F. Trendelenburg (Verhandl d Deutsch Gesellsch. f Chir 2.89, 1908). With improvements in technic and more clearly defined indications, it may be possible in the future to treat more pulmonary emboli surgically.

**GANGRENE.—Pneumothorax Treatment.**—G. dalla Torre (Polichinics (sez med) 41 157 (Mar) 1934) reports that the collapsed lung after pneumothorax in pulmonary gangrene has seldom been studied histologically. He made such a study and compared the findings in the collapsed lung with those in the one unaffected. In the diseased lung sections were obtained from the gangrenous

excavation, the adhesions, the hilus, and the hilar lymph nodes. Studies were made and reported of 5 cases in which pneumothorax was induced and of 1 case in which this treatment was not applied. The duration of the pneumothorax and the time elapsing between the development of the disease process and the institution of the pneumothorax treatment varied in this series of cases, a fact of prime importance.

The rôle of connective tissue in the healing of tuberculous foci is well established. In the cases reviewed there was an appreciable development of connective tissue, especially in the subpleural regions, the vascular adventitia, and the gangrenous foci. In the gangrenous foci there was often the development of a new peculiar lining resembling a highly vascular granulation tissue. The presence of inflammation and the continued collapse of the lung, with the subsequent relative collapse of the lymphatics and smaller blood-vessels, play an important rôle in determining the amount of new connective tissue formed. Antoniazzi, from studies with silver impregnations, concluded that this new connective tissue formation resulted from metamorphosis of collagenous tissue of the alveoli, histiocyte proliferation, and especially perivascular proliferation.

In a general way, the elastic tissue in the collapsed lung showed signs of degeneration and disintegration and in some places slight hyperplasia due probably to the toxic products of the gangrene as well as the changed physical condition of the lung. The alveolar lumen showed a fairly constant change, being reduced in the hilar regions and dilated in the subpleural areas, and contained many macrophages and mononuclear cells. The blood-vessels were moderately dilated and congested, especially the veins and capillaries, some of which were newly formed.

In many respects the pathologico-anatomical and histological changes were similar to those occurring in lungs collapsed because of tuberculosis and neoplasm. In pulmonary gangrene the degenerative process in the elastic tissue definitely predominates.

In the course of 4 years 43 cases of pulmonary gangrene were studied clinically. Of 21 cases treated by pneumothorax, 10 recovered. The ages of the patients ranged from 32 to 67 years. The time of the institution of the treatment varied from 15 days to 4 months after the onset of the disease, and the duration of the collapse from 1 to 5 months. The location of the lesion has a questionable influence. From these observations the conclusion was reached that pneumothorax is a most valuable method of treating many cases of pulmonary gangrene. Its therapeutic action is probably based on mechanical hindrance to diffusion of the gangrenous process and the passage of toxins into the circulation from the compression of the cavity. The treatment should be continued for months. Following recovery, the patients are more susceptible to pulmonary infections. A residual condition, such as bronchiectasis, may be treated later.

**HEMORRHAGE, PAROXYSMAL.**—B. S. Oppenheimer and S. P. Schwartz (Am Heart J. 9. 14 (Oct.) 1933) report that severe paroxysmal pulmonary hemorrhages, not due to intrinsic disease of the lungs, are uncommon in patients with mitral stenosis. Three cases are reported of young adults under 30 years of age, suffering from chronic rheumatic cardiovascular disease with mitral

stenosis, whose main presenting symptoms were recurrent attacks of severe pulmonary hemorrhages. The attacks were characterized at times by an "aura" with psychogenic manifestations, severe pain between the shoulder blades, and palpitation of the heart. In one patient an urticarial rash ushered in the seizures. The onset of these attacks was usually during an afebrile period and came on many years after the first evidence of rheumatic fever. The attacks themselves were characterized by dyspnea, pain, asthmatic breathing, cough, and hemoptysis. At first the expectoration was frothy in nature, but later there were frank hemoptyses in quantities of from one to several hundred cubic centimeters of blood. The lungs during such seizures showed evidences of either localized or diffuse transudation in the alveoli, and there was a characteristic x-ray picture that was often mistaken for pneumonia. The attacks would last from one hour to several days, and with their cessation the lung signs cleared up entirely.

It was impossible to prevent the onset of such seizures in these patients by any medication. **Morphine sulphate** and **atropine sulphate** administered in adequate doses following the seizures seemed to allay the fear and abate the hemoptysis.

Two of these patients died within 3 years following the onset of such recurrent attacks. In the one case with autopsy, no bleeding point could be found.

In the absence of any embolic or thrombotic manifestations in the lungs, it is probable that such seizures are the result of some reflex stimulation of the capillaries lining the alveoli, resulting in hemorrhages from diapedesis, or possibly also from rhexis of capillaries lining the walls of the bronchial tree.

**PLEURA. — Pathology.** — *Behavior in Pneumothorax* — E. Fleischner (Wien klin Wchnschr 46 1486 (Dec. 8) 1933) observed that fibrin exudation and the formation of adhesions is much more pronounced in the parietal than in the visceral pleura. He reviews cases of internal perforation of old pleural exudates in which the two pleuræ showed an entirely different behavior. He also noted that, whenever in the course of exudative pleurisy or of pleural empyema a puncture is made and air enters the cavity, the x-rays reveal that the parietal pleura is covered with a fibrinous layer of considerable thickness, while the visceral pleura shows hardly any changes. Such observations are best made on patients undergoing pneumothorax therapy. The exudate does not necessarily have to be large; on the contrary, the fibrin deposits are noticeable in cases of small, marginal exudates and even in dry pneumothorax. In children and young persons, it is frequently noted that the fibrinous layer becomes narrower as the lung unfolds again, however, indurations usually develop in adults. The author cites animal experiments by Sorgo, corroborating the severe involvement of the parietal pleura and the almost negligible changes on the visceral pleura. Sorgo, as well as Fleischner, sees the cause of this varying behavior in the different lymphovascular supply of the two pleuræ. The author points out that these observations are important for the therapy. Measures inducing hyperemia counteract the lymphatic stasis and prevent, or at least reduce, the formation of fibrinous deposits and of indurations. The respiratory gymnastics recommended by Hofbauer are helpful. In patients who have received this treatment,

the pleural indurations are usually negligible, and the author believes that the early use of active and positive muscular movements promotes the circulation of the lymph and prevents the exudation of larger amounts of fibrin on the parietal pleura.

**Sero-albuminous Expectoration Following Pleural Puncture.**—The clinical aspects are described by C. Mumme (Beitr. z. Klin. d. Tuberk. 85:20 (June) 1934). He rejects all pathogenic theories according to which the expectorate in sero-albuminous expectoration following pleural puncture is an expectorated pleural exudate. He maintains that the cause of sero-albuminous expectoration following pleural puncture is a local acute pulmonary edema, which develops in the prolongedly compressed and in the rapidly extended (during puncture) lung. Thus the expectorate is transudated blood serum. The development of the pulmonary edema following pleural puncture must be ascribed to degenerative changes on the capillary endothelium, also to mechanical and, finally, to angioneurotic factors. Epinephrine can prevent a sero-albuminous expectoration only when it is given early, *i e.*, approximately 15 minutes before the puncture is made. By introducing air into the pleural space and by thus renewing the pulmonary collapse, it proved possible to counteract a sero-albuminous expectoration and thereby save the patient. If in case of more extensive pleural punctures a part of the discharged fluid is replaced by air, the development of the pulmonary edema is prevented and with it also the sero-albuminous expectoration. The author rejects the puncture treatment of the serous "idiopathic" pleural exudates, because the measure does not reduce the duration of the disturbance. In "idiopathic" serous pleurisy, puncture should be resorted to only if, disregarding vital factors immediately following the discharge of the exudate, collapse treatment is instituted by inducing a pneumothorax.

**Diagnosis.**—*New Sign of Effusion*—E. S. Weiler (Rev. méd. del Rosario 24:700 (July) 1934) considers Koranyi's sign (hypophonesis of the dorsal segment on direct percussion of the apophysis of the dorsal vertebræ) of diagnostic value in pleural effusion. The mechanism of the sign is explained by the interposition of the pleura, filled with liquid, between the lateral and ventral aspects of the vertebræ and the lung. The sign may also be present without pleural effusion in bilateral hepatization of that portion of the lung adjacent to the dorsal vertebræ and in intrathoracic tumors, when they are in contact with the lateral and ventral aspects of the dorsal vertebræ. To differentiate the presence of pleural effusion from that of either intrathoracic tumors or bilateral hepatization of the lung, the author has determined the hypophonesis of the dorsal segment during the changes of position of the patient. The upper limit of the hypophonesis is verified by means of the direct percussion of the dorsal apophysis and then marked, first with the patient standing or sitting down (classic technic) and then with the patient in abdominal decubitus. In cases of pleural effusion the upper limits of the vertebral hypophonesis descends one, two or more inter-spinous spaces. The author calls the sign "descent of the vertebral hypophonesis." Its mechanism is explained by the mobilization of the intrapleural liquid, leaving the pleura between the lung and the dorsal and ventral aspects of

the vertebræ more or less empty during abdominal decubitus. When the pleural effusion is not great and there is no hepatization of the lung, the vertebral column recovers its normal resonance along its whole length (positive hypophonic disappearance). The absence of modifications of the vertebral resonance during the changes of position of the patient (negative hypophonic descent) indicates an absence of pleural effusion. The sign is not equivalent to Grocco's triangular area and frequently shows itself without the existence of such an area.

**Treatment.**—*Simplified Oleothorax.*—A. Josewich (M. Bull. Vet. Admin. 10 173 (Jan.) 1934) feels that the simplification of technic and the use of colloid materials may lead the profession to a more general acceptance of oleothorax treatment. Liquid petrolatum of the best quality should be employed. A choice may be made of aromatic oils or antiseptics to be added to the liquid petrolatum. The author uses oil of cajuput, U. S. P. X, rectified. It is well to incorporate, as necessary in proper amount, various dyes or antiseptics to assist in the early detection of pleuropulmonary perforations or to add antiseptic properties to the solution. The principal change in technic is the use of a preparation in colloid form. Any disinfectant value which may be ascribed to the substances employed is based on the proposition that, to be effective, a disinfectant must be absorbed by the bacteria. Since any of the injections may result in reactions, it is considered advisable to inject from 1 to 4 c.c. ( $\frac{1}{4}$  to 1 dram) of a 1 to 5 per cent solution of the essential oil in liquid petrolatum as the initial dose. In contrast to the use of the ordinary oil, the colloid solution will permit of the use of needles of the smallest caliber. Subsequent quantities are injected in arithmetical progression at intervals of one week or longer. If pus is present, moderate amounts should be removed at each treatment. Overenthusiasm must not be exercised about obliterating the pneumothorax pocket, as the persistence of a small air pocket serves as a buffer in the event of increased hydraulic pressure due to the production of exudates resulting from irritation of the pleura by the oil. This lessens the possibility of perforation and tearing. The most reliable means of checking the status of the oleothorax is fluoroscopic control before and after the injection of the oil, as well as in the interim. Manometric readings are usually obtained, but they may be and frequently are misleading and subject to alarming change within a few minutes or hours.

**PLEURAL ADHESIONS.**—**Treatment.**—As cauterization of pleural adhesions has become more frequent and more complicated, **anesthesia** has more often become necessary. To overcome the difficulties in this connection O. Haave (Norsk. mag. f. lægevidensk. 95 275 (Mar.) 1934) has devised a stiff cannula of the form and size of the cautery and ending in a point 3 cm. long and at the handle end in a 5 c.c. syringe. If anesthetization is called for, the cautery is readily replaced by this cannula, the same field of vision is kept, and certain anesthesia is attained.

**PNEUMONIA.**—**Etiology.**—*Pneumococcus Carriers*—E. A. Bliss, W. D. McClaskey, and P. H. Long (J. Immunol. 27·95 (July) 1934), in an effort to determine whether the constant carrying of pneumococci in the throat was asso-

ciated with frequent infections of the upper respiratory tract, obtained throat cultures from a group of 20 young adults approximately once a week over a period of 2 academic years. Of the 1016 throat cultures that were obtained, 34.5 per cent were positive for pneumococci. After the first year it seemed that individuals could be divided into 3 groups with respect to the carrying of pneumococci, *i. e.*, chronic carriers, intermittent carriers and noncarriers. However, at the end of the second year it became apparent that those individuals who had been classed as intermittent carriers were, in reality, chronic carriers, for, although few positive cultures were obtained from them, and those irregularly, the same type of pneumococcus recurred in their cultures. It was found that there was little difference in the frequency and duration of infections of the upper respiratory tract between the chronic carriers and the noncarriers. While the same type of pneumococcus tends to recur in the throat cultures from a chronic carrier, it is frequently possible to demonstrate the simultaneous carrying of 2 or 3 types of pneumococci in these persons if the proper procedures are used. The authors believe that their study adds evidence in favor of the theory of the stability of pneumococcus types in the human being.

*Aspiration of Oil*—D. M. Grayzel and J. J. du Mortier (Yale J. Biol. and Med. 6: 599 (July) 1934) report 2 cases of pneumonia in children following the aspiration of oil or fat. Pinkerton studied the lesions produced experimentally in animals by intratracheal injections of various oils of animal, vegetable or mineral origin, and found that the resulting lesions varied with the type of oil used. The animal and mineral oils called forth a marked proliferative response on the part of the tissue, whereas practically no response resulted from the intratracheal injection of vegetable oils.

*Lipoid Cell Pneumonia*.—T. C. Goodwin (Am. J. Dis. Child. 48: 309 (Aug.) 1934) observed 25 cases of lipoid cell pneumonia during the past 10 years. In 3 of these the diagnosis was established clinically, in the others, at necropsy. The ages of the children ranged between 6 months and 5 years. Various oils were responsible. *Milk fat* was perhaps found most frequently. The children were weak or comatose and were fed by gavage, or vomited frequently, and the regurgitation of the milk was the cause of the aspiration. *Cod-liver oil* was present in the lungs in a number of infants, and in almost all there was the history of cough, vomiting or struggling against the administration of the oil. In 4 of the cases in which the amount of pulmonary involvement was the greatest, a clear history of the instillation of *liquid petrolatum* in the nose, or its ingestion, was obtained. The oil was identified in the lung in 2 instances.

*Symptoms*—Rapid respiration without dyspnea and a persistent hacking cough stand out as the two most frequent complaints.

*Diagnosis*—A single roentgenogram is scarcely ever typical enough to do more than suggest lipoid cell pneumonia. The course of the disease is in most cases determined by the condition associated with it. There is as great a difference in the pathologic picture found at necropsy in cases of lipoid cell pneumonia as there is in the clinical picture. It should be suspected in small, debilitated infants who fail to gain weight and who have a chronic cough and rapid respiration. These symptoms, in the absence of fever, suggest lipoid cell pneu-



monia Tuberculosis must be ruled out. The blood picture is normal in uncomplicated instances and is in conformity with the picture of coincident infections. The x-ray picture is of the greatest help. The consolidation is central, bilateral, more extensive on the right and apt to be posterior. The x-ray shadow is always more extensive than the amount of consolidation suggested by physical examination. X-rays taken weeks apart may show scarcely any difference in the appearance of the lungs. The author has never seen cavitation in lipid cell pneumonia or calcification in the bronchial lymph nodes. The tendency for the lesion to disappear gradually makes the picture unlike that of a neoplasm or congenital malformation, and the physical signs are rarely those of atelectasis.

*Prognosis.*—Uncomplicated lipid cell pneumonia offers a good prognosis.

*Treatment.*—**Good nursing with a frequent change of position and the avoidance of infection of the upper respiratory tract** is the only treatment. It is unwise to use drops of oil in the nose of any small or weak infant, and liquid petrolatum as a cathartic should not be given. When cod-liver oil is taken poorly, it is best to substitute one of the more concentrated vitamin D preparations. Care in feeding and gavage done only by experienced persons will decrease the incidence of pneumonia from the aspiration of foodstuffs.

*Treatment.*—**Human Immunization Against Pneumococcus.**—Following ingestion of pneumococcus vaccines, about 75 per cent of the persons tested by V. Ross (J. Immunol. 27: 307 (Sept.) 1934) formed protective antibodies against Type I and about 60 per cent against Type II. The results for Type III are approximately the same as for Type II. Antibodies for Type I have been found in most of the serums examined from 7 to 14 months after the oral administration of the vaccine. The indications are that the duration is the same for the 3 types. The protective substances appear promptly, being present within from 2 to 3 days following 6 feedings. The number of feedings employed has varied from 2 to 10. In one instance when 2 doses were given, antibodies were formed. In some cases 10 doses elicited no response. A new set of feedings was followed by the appearance of protective substances in the blood of about 50 per cent of such cases. It is estimated that a practical procedure would employ the pneumococci from 1200 c.c. of growth per type on each of 6 to 10 successive days, the bacterial content being estimated at  $10^9$  per c.c. The use of completely autolyzed cultures, which contain several times as much antigenic material as the bacteria present in a growth of 18 hours, would reduce proportionately the volume of broth to be handled. None of the several forms in which the vaccine has been prepared have proved superior to the others. The concentration of antibodies formed is generally such that 1 c.c. of serum will protect a mouse against 5000 fatal doses of pneumococci (Types I and II). It is believed that these protective substances indicate a generalized resistance to the pneumococcus. Agglutinins have not been detected in serums in which protective antibodies have been found. Natural protective antibody against Type I has been found in fairly large amounts in 10 per cent of the serums examined and in smaller amounts in 20 per cent more, in the case of Type II the figures were 41 and 18 per cent, for Type III, 31 and 50 per cent.

*Artificial Pneumothorax.*—F. G. Blake, M. E. Howard, and W. S. Hull (Tr. A. Am. Physicians 49. 119, 1934) report on the treatment of 22 cases of pneumococcal lobar pneumonia by artificial pneumothorax. Of the 31 cases recorded in the literature, exclusive of infants and young children, in only 16 cases was treatment begun on or before the fourth day of the disease. However, in the 22 cases herein reported, in which all but 1 case were treated before the fifth day, the majority were treated on the second and third days. The number of artificial pneumothorax treatments given, as reported in the previous literature, has been either 1 or 2, with the exception of 1 patient, who received 3 treatments. The intervals between treatments have varied from 12 to 48 hours. The amount of air introduced into the pleural cavity at each treatment has varied from 50 to 750 c c, but in most instances has been from 300 to 500 c c. In these 22 cases, the procedure has differed in that more treatments at more frequent intervals were given and larger amounts of air were introduced.

The cases were carefully selected, typical, early unilateral lobar pneumonia of pneumococcal origin, with 3 exceptions. The observations made, in addition to the usual clinical records, included serial anteroposterior and lateral x-ray pictures of the lungs at frequent intervals, repeated measurements of interpleural pressure with record of inspiratory, expiratory and mean pressures, and serial blood cultures, titrations of humoral antibodies and white blood cell counts.

The cases were divided into 3 groups, as follows. Group I, cases *without* preexisting fibrous pleural adhesions, 11 in number, Group II, cases *with* preexisting fibrous pleural adhesions resulting from previous attacks of pneumonia or pleurisy, 8 in number, and Group III, late septicemic cases with advanced consolidation, 3 in number, treated not with any expectation of benefit, but to help define the indications and contraindications for pneumothorax treatment. None of the 3 cases in Group III showed any beneficial response and all 3 died.

The method of procedure used and the results obtained will be illustrated by presentation of the data on selected cases from Group I. At the beginning it was thought that a selective collapse of the involved lobe induced by means of 2 or 3 pneumothorax treatments of 300 to 500 c c each in the course of 24 hours might be sufficient to accomplish the desired result, and this happened to be the case in the first 2 patients treated. It soon became evident, however, that a selective collapse was not necessarily obtained and that with a falling interpleural pressure relapse was liable to occur.

In view of this, the procedure was changed. The first 3 treatments were given at approximately 4-hour intervals, a sufficient amount of air being introduced to establish as rapidly as possible, without serious inconvenience to the patient, a positive expiratory pressure with a mean pressure in the neighborhood of 0 to +1 cm. of water. The total amount of air introduced in these first 3 treatments has varied from 1700 to 2100 c c, resulting in a complete compression of the whole lung on the involved side without significant shift of the mediastinum. Subsequent treatments have been given in an effort to maintain a positive interpleural pressure and compression of the lung until permanent recovery seemed assured and the danger of relapse improbable. It should be noted that temporary exacerbations of dyspnea may and sometimes do result

GROUP I CASES OF LOBAR PNEUMONIA WITHOUT PREEXISTING FIBROUS PLEURAL ADHESIONS

Case	Sex	Age	Pneum type	Site	Blood culture	Calendar day	Hours after onset	No of treat	Total amount of air, c c	Result		Complications
										Recov by	Day	
W M	M	63	IV	L L	—	2	9	10	3425	Crisis	2-3	None
W L	M	32	I	L L	—	2	24	5	2700	Crisis	3-4	Toxic psychosis.
R F	M	20	V	L L	—	2	26	6	2450	Lysis	4-7	None.
A M	F	33	I	L L	—	2	30	3	1600	Crisis	5	None
V G	F	30	I	R U	—	3	31	8	2775	Crisis	5	None
F H	M	39	XII	R U M L	+	3	38	10	3625	Lysis	4-6	Sterile pleural effusion.
A C	M	25	I	R L	—	3	54	3	1050	Crisis	4	None.
T F	M	47	XXVIII	R L	—	3	56	6	3300	Crisis	3-4	None
R D	M	44	V	R U	—	3	60	2	750	Crisis	4	None
J F	M	17	VIII	L L	—	3	61	3	950	Crisis	4-5	None.
F R	F	35	V	R U	—	4	78	2	600	Crisis	7	None

GROUP II CASES OF LOBAR PNEUMONIA WITH PREEXISTING FIBROUS PLEURAL ADHESIONS

Case	Sex	Age	Pneum type	Site	Blood culture	Calendar day	Hours after onset	No of treat	Total amount of air, c c	Result		Complications
										Recov by	Day	
H T	M	36	II atyp	R L U	—	3	46	3	1000	Crisis	8	None.
M. C	F	28	I	R U	—	3	50	5	2075	Crisis	5	None.
J H	M	32	I	R U.	—	3	52	3	1850	Crisis	6	None.
D G	M	37	I	L L	+	3	54	2	550	Recovered	...	Empyema.
B G	M	30	I	R L	—	4	64	3	2300	Recovered	...	Empyema.
W S	M	13	II	R L → R M	—	4	66	3	1085	Crisis	8	None.
M S	M	54	V	R M → U	—	4	80	6	3100	Crisis	8-9	None.
S C.	F	36	V	R L.	—	4	82	5	2300	Crisis	7	None.

GROUP III LATE SEPTICEMIC CASES OF LOBAR PNEUMONIA

Case	Sex	Age, years	Pneumo Type	Site	Blood culture	Calendar day	Hours after onset	No. of treat.	Total amount air, c c.	Result
J G	M	41	I	R U M L	+	4	84	1	350	Died, 5th day
J. L.	M	77	VIII	L L	+	5	90	3	675	Died, 6th day
S M	F	48	IV	R. L.	+	4 + ?	90 + ?	5	2000	Died, 6th day

from this procedure, but in themselves these are not alarming if pleural pain has been relieved, the spread of the pneumonia has been checked, and the fever and toxemia have been abated, as seems to be the case.

Although the 22 cases reported are too small a number to warrant any definite conclusions, it would appear that artificial pneumothorax, if given early and at sufficiently frequent intervals with adequate amounts of air to establish rapidly and maintain a slightly positive mean interpleural pressure, gives promise of being a very valuable therapeutic procedure in cases of lobar pneumonia without preexisting fibrous pleural adhesions. It is obviously desirable to confirm these results so far obtained by a larger series which will include cases of pneumococcus Type II and Type III pneumonia and early cases with bacteremia. Whether the method will be of some value in cases with preexisting pleural adhesions in perhaps reducing mortality, if not shortening the course of the disease, remains to be determined. There is no indication that it will be useful in late septicemic cases with advanced consolidation of the lungs. It seems probable that the beneficial effects of artificial pneumothorax are largely due to early compression and immobilization of the acutely inflamed lung.

*Discussion*—Well into the third day of the disease the inflammatory process in the lung is largely an interstitial inflammation with perhaps some edema in the alveoli, without much actual consolidation. If one wished to use a descriptive term, the early process might be called an erysipelas of the lung. That is probably the reason why it is so easy to compress the lung so much during the early stage of the disease.

There is no means of determining whether fibrous pleural adhesions exist or not prior to the introduction of air. A previous history of pneumonia indicates that they may be expected to be present in such cases and this is established by x-ray examination after the first 2 or 3 injections.

In the cases without pleural adhesions there was no evidence in any of further spread of the pneumonia to any other lobe. In 2 cases with adhesions, spread did occur to another lobe, in 1 case to a lobe on the opposite side, in the other case, from the middle to the upper lobe on the right.

The attempt is made to collapse completely all lobes on the involved side. The original notion that a selective collapse of the involved lobe was all that was necessary has been abandoned.

**RESPIRATORY TRACT.—Treatment.**—*Artificial Respiration, Rocking Method*—E. M. Killick and F. C. Eve (Lancet 2 740 (Sept. 30) 1933) compared the tidal air induced in artificial respiration by rocking on the stretcher with that produced by Schaefer's method. The comparison indicated that the rocking method is at least as effective as any of the manual methods. The rocking method has the advantage over the prone pressure method of requiring less exertion in performing the necessary movements. Therefore, artificial respiration can be maintained more easily over long periods. The method may be applied by an untrained operator, following simple instructions as to timing. Warmth, a factor so important and so commonly neglected, can be adequately applied. Investigation of the circulatory changes induced by the rocking method show that their

magnitude is not such as should be of clinical importance. As to the variations in the gaseous exchange with different rates of rocking, the figures show that at rates above 15 times per minute there is a tendency to overventilate and hence wash out carbon dioxide in amounts disproportionate to the amount of oxygen that can be absorbed. Since carbon dioxide is an important stimulus to the normal activity of the respiratory center, the onset of spontaneous breathing might be delayed if its amount in the blood should be reduced too far. Since measurements by Silvester's method of lung ventilation show that rocking the stretcher 10 or more times a minute induces adequate ventilation, the authors conclude that for most subjects the optimal rate of rocking the stretcher lies between 10 and 15 times per minute, *i. e.*, the normal rate of breathing. In practice, Schaefer's method must be tried without delay and used until the rocking stretcher with blankets and hot-water bottles can be brought and employed if resuscitation is delayed or inadequate.

F. C. Eve (Lancet 2:995 (Nov. 5) 1932) described the method as follows: The unconscious patient is placed face downward on a pivoted rockable stretcher, which is rocked 45° up and down. The weight of the abdominal viscera in the head-down position pushes the diaphragm up into its expiratory phase. In the feet-down position, inspiration is similarly produced.

*Effects of Drugs on Ciliary Activity of Upper Respiratory Tract*—D. M. Lierle and P. M. Moore (Arch. Otolaryng 19:55 (Jan.) 1934) determined the effects of certain drugs on the ciliary activity of strips of tissue mounted in a special microscope chamber and the effects of a larger number of drugs on the ciliary activity of the unbroken mucosa of the turbinates of freshly killed guinea-pigs. They observed that *tap* and *distilled water*, when applied to the mucosa of the upper respiratory tract, cause slowing of the ciliary beat. A 3 per cent solution of *ephedrine hydrochloride* is not detrimental to ciliary activity but at times increases it slightly. A 5 per cent solution of *cocaine hydrochloride* is not detrimental to ciliary activity, but 10 and 20 per cent. solutions produce definite slowing, with good recovery. *Mild silver protein* in concentrations of 5, 10 and 20 per cent produces an initial speeding of ciliary activity. This is followed by a slowing, which may be due to the water solvent rather than to the drug. A 0.5 per cent solution of *eucalyptol* has no deleterious effect on ciliary activity. A 0.5 per cent *menthol* and, to a greater degree, 1 per cent *menthol*, have a mildly depressing effect on ciliary activity. *Thymol* in 1 and 0.5 per cent. concentrations and 1 per cent *eucalyptol*, in the order named, are definitely detrimental to ciliary activity. A 1:1000 solution of *epinephrine hydrochloride*, 2 per cent *zinc sulphate* and 2 per cent *mercurochrome*, in the order named, are definitely detrimental to ciliary activity. *Silver nitrate* in 0.5 per cent concentration is immediately and fatally detrimental to ciliary activity. In no instance was it possible to start the cilia beating again after its application.

**TUBERCULOSIS.—*Etiology.***—In a study of the relation, if any, between *sunbathing* and pulmonary tuberculosis made by A. H. Gosse and G. S. Erwin (Brit. M. J. 2:15 (July 7) 1934), careful inquiry in each case elicited the fact that, out of 66 cases of tuberculosis admitted to a hospital between August and

December, 1933, the onset or exacerbation of symptoms in 11 cases followed sunbathing. The age incidence ranged between 19 and 33 years, the period of life common to sunbathing and to the production of the exudative type of the disease. On x-ray examination, this exudative type of pulmonary tuberculosis was found to be present in the 11 cases. Although there was a considerable proportion of the fibroid type of disease among the other 55 patients, each one of them denied indulging in sunbathing during the summer, and an absence of sun pigmentation supported their statements as far as it could. The fibroid type was present in some patients whose age was greater than the average of sunbathers, and in others who had passed the exudative stage. Many of these patients had a long history of tuberculosis and had been deliberately warned by their physicians against the danger of sunbathing. That the abnormal exposure of the usually covered skin surfaces to the action of the sun's rays aggravates the development of pulmonary tuberculosis is a conclusion suggested by these 11 cases. It is believed that this new social custom has elements of danger if indulged in extensively and indiscriminately. The exact manner in which sunbathing may aggravate tuberculosis is not understood, *i. e.*, whether long sunbaths raise the body temperature in healthy young adults or possibly only in those in a hyperallergic state. For the latter possibility there is some support in the fact that several patients showed an immediate reaction in the form of malaise and sweats, as well as a delayed reaction from some weeks to 3 or 4 months later, in the more dramatic form of hemoptysis among other symptoms.

**Pathology.**—A. G. Emslie (Edinburgh M. J. 41:141 (Mar.) 1934) made 54 blood cultures and 28 animal inoculations (omitting 2 animals that died within 2 weeks) for *tubercle bacilli in the blood* of 34 known tuberculous and 4 non-tuberculous patients, and in 2 cases some result other than a definite negative has been found. Two cases produced acid-fast bacilli which failed to infect guinea-pigs. As both subculture and animal inoculation with scrapings of the cultures showing acid-fast bacilli failed, it is impossible to regard them as tubercle bacilli. All animal inoculation tests were negative. Reexamination at a later date of the cultures containing acid-fast bacilli revealed that they had disappeared from the culture. The occurrence of any degree of continuous tuberculous bacillemia was not proved. Acid-fast bacilli are found in cultures by various methods, the proportion varying with the different investigators. By the above method a percentage of 5.3 was obtained. The exact nature and source of these acid-fast organisms was not determined, but it is highly probable that they are contaminations from sources such as glassware and tap-water. Loewenstein's medium is suitable for the culture of tubercle bacilli. Loewenstein's results have not been confirmed by the author, whose work agrees with the observations of Schwabacher, Weatherhall, Cumings and Pearce.

**Clinical Course.**—**Primary Tuberculous Infection.**—The concept of C. A. Stewart (Nebraska M. J. 19:321 (Sept.) 1934) relative to the evolution of tuberculosis in the human lung from the first infective phase to the final stage of far advanced phthisis implies that the first infection makes possible rather than prevents the development of the adult type of tuberculosis. When other serious reinfective forms of the disease are considered, these conditions, which develop

as the result of the discharge of bacilli from preëxisting primary foci of disease, are seen to be caused often by the dissemination of direct descendants of the initial infective dose of tubercle bacilli that entered the body. There is no form of tuberculosis to which man is susceptible that is prevented by the first invasion of the tissues by tubercle bacilli. In fact, the primary infection is the first step along the path which leads too often to the development of all the serious reinfective varieties of tuberculosis that menace the human race. As a result of several years' study, a negative tuberculin reaction is considered superior to a positive one and the nonallergic, uncontaminated person is considered in a more advantageous position than the infected person, so far as future experiences with tubercle bacilli are concerned. The prediction is ventured that in the near future an initial infection with tubercle bacilli will be generally accepted as a hazardous liability rather than a protective asset, and a deeper appreciation will arise relative to the soundness and value of campaigns fostered by national, state and local tuberculosis associations directed toward the prevention and final control of tuberculosis.

*Virulence of Tubercle Bacillus*—Exploratory punctures were made by Y. Nedelkovitch (Presse méd. 42. 619 (Apr. 18) 1934) on 11 patients to determine whether in the spontaneously disappearing tuberculous exudates the fluid becomes bactericidal outside the organism. Each specimen was left for a longer or shorter period either at the laboratory temperature or that of the incubator. The material was injected into guinea-pigs. In all instances, positive evidence of live and virulent tubercle bacilli was obtained. Therefore, the conclusion is drawn that tubercle bacilli are not dead in disappearing exudates and that convalescence and cure result in spite of the presence of living virulent organisms. Recovery, therefore, depends not on the presence of bacilli in the exudate, but on the relation between the bacilli and the cells (and probably other elements) in the pleural lesions themselves. In the purulent pleurisies of pneumothorax which disappear spontaneously and in which the recovery takes a long time, the specimens taken toward the end lose their virulence much more rapidly than those obtained at the early appearance of the exudate. Furthermore, it was apparent that the bacilli in the exudates were just as resistant to the bactericidal properties of the exudate outside the body as inside. These bacilli, however, become sensitive to this bactericidal action of the exudate after passage through culture mediums. When recovery begins, the organism becomes insensible to the poisonous effect of the bacteria, but the bacilli also are resistant to the bactericidal action of the tissues. In making repairs, the organism clears out the bacilli in the same way as it does cellular débris or foreign bodies. Thus, the enormous number of bacilli disappear, although some may persist and can produce new lesions in case of returned lowered resistance on the part of the host.

*Complication.—Tuberculous Rheumatism*—As described by E. A. Brav and P. S. Hench (J Bone and Joint Surg 16 839 (Oct.) 1934), this condition is a form of polyarthritis, simulating in some cases acute rheumatic fever or in other cases chronic atrophic arthritis, but bearing some suggestion of tuberculous etiology. Familial tuberculosis, associated visceral tuberculosis, demonstration of Koch's bacilli in the synovial fluid and in the blood stream,

positive results of inoculations of guinea-pigs with joint fluid and, in some cases, the presence of a typical tuberculous joint before, coincident with, or subsequent to the development of polyarthritis, have been considered evidence for the diagnosis of tuberculous rheumatism. The condition is thought to be due to a tuberculous toxin from some distant focus, a filtrable virus, an attenuated form of bacilli of tuberculosis or an allergic reaction. Formation of true tubercles, therefore, is not the expected finding and, when such pathologic change is present, a superimposed tuberculous arthritis, rather than the condition of tuberculous rheumatism, is thought to exist.

Against the acceptance of the syndrome of tuberculous rheumatism have been arrayed a large number of competent investigators who have argued that there is no adequate clinical method of identifying it, no consistently characteristic x-ray evidence, no experimental or laboratory evidence in its favor that is not highly controversial, and no consistent demonstration of any characteristic microscopic pathology. A statistical study of a series of 150 cases of acute rheumatic fever and 250 cases of chronic atrophic polyarthritis has revealed no significantly higher incidence of familial tuberculosis or associated visceral tuberculosis than that found in a group of 250 control cases. Of a series of 75 cases in which a diagnosis of chronic atrophic polyarthritis had been made and in which the pathologic characteristics of a single joint were determined by microscopic examination of tissue or inoculation of guinea-pigs, 8 patients were found to be definitely tuberculous. In each of these the tuberculous identity of the joint was suspected prior to the examination of the tissue or inoculation of guinea-pigs, but the association with multiple arthritis was confusing.

*Influenza*—The course of an influenza epidemic in a sanatorium for tuberculous patients was observed by L. Mandel (*Beitr. z. Klin. d. Tuberk.* 84: 473 (Apr. 20) 1934). The epidemic was comparatively mild, since of the 104 patients, none developed complications. In different influenza epidemics the course of the infection as well as the complications show a certain variability. This may explain the difference in opinions about the effect of influenza on tuberculosis. In the 104 patients, 11.25 per cent. developed considerable exacerbations, aside from mild impairments detectable only by laboratory methods. Tuberculous patients should be protected against influenza as much as possible. If in spite of all precautions a tuberculous patient develops influenza, he should be carefully watched during and after the attack, so that an exacerbation will be discovered immediately and proper therapeutic measures may be taken. The influenza-like disturbances developing after epidemics should be given particular attention, since they frequently mask a tuberculous relapse or an early infiltrate.

*Exudative Pleurisy in Course of Artificial Pneumothorax*—M. Belli (*Clin. med. ital.* 65: 263 (Mar.) 1934) observed the beneficial influence of a pneumothorax pleurisy on tuberculous pulmonary cavities in 7 patients in whom pneumothorax was not effective and after exudative pleurisy occurred. In considering the duration of the pneumothorax of the same type at the time in which the parenchymal alterations took place, there is a relation of cause and effect between the exudative pleurisy and the facts observed. X-ray, clinical and bacteriologic studies impel to the advancement of the hypothesis that there had been a true



and actual cure of the tuberculous cavities corresponding to the disappearance indicated by means of the x-rays. It is difficult to confirm such a cure with certainty during a lifetime. These difficulties are increased in the described cases by the absence of observations on reexpanded lungs. In all cases, a subjective and objective improvement was demonstrated in addition to the disappearance of the tubercle bacilli from the sputum. Concerning the mechanism of pneumothorax, there is an inclination to attribute to exudate pleurisy a complex of mechanical and immunizing factors favoring histogenous immunity. The therapeutic utilization of these effusions may offer marked benefits that the pneumothorax alone could not produce.

**Diagnosis.—Bronchography.**—J. E. Murphy (Am. J. Roentgenol 31:301 (Mar) 1934) reports on 65 of 99 cases of pulmonary tuberculosis which were studied with the x-rays following the intratracheal injection of lipiodol. Of 56 cases in which cavernous lesions were present, 66 per cent. showed definite bronchial dilatation; 7 per cent., bronchial distortion without dilatation; and 2 per cent., a suggestion of bronchial dilatation. The incidence of bronchial dilatation was highest, 73 per cent., in the cases of mixed cavernous lesions, next highest, 60 per cent., in cases of fibrocavernous lesions; and 25 per cent., in cases of caseocavernous lesions.

In cases of infiltration the incidence of bronchial dilatation was 43 per cent. The infiltrated lesions associated with dilatation were all predominantly productive.

In 80 per cent. of the 40 cases showing bronchiectasis, the dilatation was limited to the upper lobe. In the remaining 20 per cent., two or more lobes were involved. Involvement of more than one lobe was as frequent in cases of caseocavernous lesions as in those of fibrocavernous lesions. In an occasional case, tuberculosis confined to one lower lobe was associated with bronchiectasis.

In 25 per cent. of the 56 cases of cavitation the cavities were penetrated by the lipiodol.

A lower lobe retracted so that it was represented in the x-ray picture by a small triangular area of density in the cardiophrenic angle was observed in 5 (7 per cent.) of the cases. Of these, 4 showed bronchial dilatation in the retracted lower lobe. Bronchiogenic spill-over of tuberculous infection was suggested or proved in 4 cases. In 2 cases the spread was from the contralateral lung.

The method of examination described has the following indications:

1. The interpretation of the pathology of tuberculosis

- (a) As bronchial dilatation is frequently present in tuberculosis and its x-ray manifestations may simulate those of parenchymal disease, its differentiation is often necessary to determine the treatment indicated.

- (b) Baffling areas of density and rarefaction may be resolved into a logical part of the pathological picture.

2. The surgery of tuberculosis. It permits the differentiation of parenchymal cavities from bronchial dilatations and, when collapse is to be practiced, the determination of the lung involved and accurate localization of the cavity.

3. To explain productive cough with a negative sputum.

The *limitations* of the method include difficulty in penetrating cavities with the lipiodol due to diseased and tortuous bronchi-containing, obstructing secretion. However, as secretion in healthy bronchi may prevent filling, mere failure of the bronchi to fill does not necessarily indicate bronchial disease. In some cases the amount of lipiodol used may be insufficient to penetrate the diseased area.

Apparently slight dilatation of the bronchi in the inspiratory phase may be incorrectly interpreted as pathological when the expiratory phase may show the bronchial tree to be normal.

The method is *contraindicated* by:

- 1 Acute pulmonary tuberculosis accompanied by fever.
- 2 Debility rendering the extra exertion required by the examination inadvisable.
3. Recent hemorrhage. In cases of recent hemorrhage it is best to delay the examination for from 8 to 10 days.

The iodine apparently does not exert a harmful effect on the course of the disease. While several untoward results are cited, check-up by x-rays at varying intervals following the injection of the lipiodol revealed no progression of the lesions.

In the majority of sanatorium patients tuberculosis is a bronchopulmonary rather than a purely pulmonary disease. The bronchial element can be recognized only in bronchograms. Hence, for correct interpretation and treatment of the bronchopulmonary lesions it is essential to outline the bronchial tree.

*Diagnostic Value of A-O*—Y. Yoshida (Eighth Session Jap Med A, 1930) reported a specific tuberculosis diagnostic method. The principle is that the injection of A-O occasions certain prescribed movements in the number of leukocytes in the blood of the recipients, according to whether or not they are tuberculous. By observing this movement Yoshida claims that it can be determined whether they are tuberculous, and if so, whether the disease is active, and also the prognosis.

*X-ray Micronodular Images*—J. Dutrey (Prensa méd argent 21 787 (Apr) 1934) states that the x-ray micronodular images of the tuberculous lung may be due to certain forms of fibrous tuberculosis or be caused by bronchial aspiration of blood during hemoptysis, without having in any case any relation to miliary tuberculosis. The intrapulmonary localization of blood after hemoptysis follows, as a rule, a benign evolution, but some fatal cases may occur. There are cases in which the posthemoptysic micronodular shadows, instead of being reabsorbed in a few months, remain, definitely giving the impression of having been transformed into a chronic miliary tuberculosis of bronchogenic origin. The existence of chronic miliary tuberculosis cannot be denied, since the presence of the disease has been proven in some necropsies. Chronic miliary tuberculosis, Banzancon nodular fibrous tuberculosis and the intrapulmonary bronchogenic repletion of hemoptysic blood have similar clinical and x-ray characteristics, which make a differential diagnosis difficult. There are many nontuberculous pulmonary diseases, such as influenza, syphilis, tumors, pneumonokoniosis, miliary bronchopneumonia and cardiac diseases, capable of

producing x-ray micronodular shadows of the lung so similar to those given by miliary tuberculosis that it is nearly impossible to make an exact differential diagnosis by the simple x-ray examination of the lung. Confusion arises even when the two anatomic parts are held and observed together. It has been noted that the shadows attributed to miliary tuberculosis which followed a favorable evolution probably were produced by the nontuberculous diseases. Since the micronodule is the fundamental lesion which appears in the x-ray picture of all the aforementioned tuberculous and nontuberculous diseases, the term "granulia" should be replaced by the term "micronodulia," which includes all pulmonary micronodules of both tuberculous and nontuberculous etiology, and also because the new term would not suggest any etiologic or anatomic concept as does the word "granulia."

*In Children.*—H. V. Morlock and A. J. S. Pinchin (Lancet 1:1114 (May 27) 1933) consider epituberculosis in reality atelectasis caused by enlarged hilum nodes pressing upon a bronchus.

The characteristics of epituberculosis are: (1) Occurrence in childhood; (2) unproductive cough; (3) sputum and feces negative for tubercle bacilli; (4) positive tuberculin reaction; (5) physical signs consisting of dullness, increased vocal resonance and bronchial breath sounds, all limited to the upper lobe; (6) the x-rays show a homogeneous shadow extending from hilum to parietal pleura, filling the apex and limited below by the interlobar pleura; (7) recovery with complete disappearance of the lesion and physical signs

*Differential Diagnosis.*—Two cases are reported by A. A. Karan and W. Haymaker (Am J Roentgenol 32:322 (Sept) 1934) in which a mistaken diagnosis of *pneumothorax* was made—one a case of tuberculous vomica occupying almost an entire lung, the other a case of an immense emphysematous bulla. In both cases necropsy was performed. In the first case physical examination was of little aid in arriving at a correct diagnosis. It tended to confirm the presence of pneumothorax suggested by the x-ray picture. Iodized poppy-seed oil instillations might have been of value, for it would have shown the defects in the bronchial tree and would have collected entirely on the floor of the excavation. On the other hand, if the pathologic picture had been that of a tuberculous pneumothorax with bronchopleural fistula, the iodized oil would have passed through the fistula and settled on the floor of the pneumothorax cavity. The patient was too ill for bronchoscopic examination. Aspiration would have been of value if the condition had been that of closed pneumothorax. However, it could not have differentiated a giant cavity from a pneumothorax with bronchopleural fistula. The patient had no hemoptysis or even blood-tinged sputum throughout the course of the disease. In the second case, bronchoscopy with iodized poppy-seed oil instillation would have been of diagnostic value for the reason that a bronchial tree could have been demonstrated within the wall of the emphysematous sac. A view of the roentgenogram in retrospect does cast some doubt on the diagnosis, because there is no distinct demarcation between the area of decreased density and the pulmonary tissue. If the diagnosis had been doubted, x-rays taken in lateral and oblique positions might have been of

diagnostic value. Instillation of the iodized oil should be used as a routine measure in doubtful cases of pneumothorax.

**Treatment.** — *Artificial Pneumothorax.* — Gaseous distention of the retrosternal pleural pouch in therapeutic pneumothorax is discussed by R. Grandgérard and P. Weber (Arch. méd. chir. d. l'app respir. 8:477, 1933). Mediastinal hernia occurring during artificial pneumothorax causes symptoms of dyspnea, pain and cardiac disturbance. To relieve the patient, the pneumothorax cavity should be aspirated and the pneumothorax carefully continued with refills of smaller amounts under reduced pressure and at longer intervals. There are 2 weak spots in the mediastinum, the upper lying between the first and third ribs anteriorly and the lower between the fifth and tenth dorsal spines posteriorly. In most cases hernia occurs in the upper and anterior mediastinal weak spot. Hernia has been observed in the presence of highly positive intrapleural pressure and of definitely negative intrapleural pressure. Some lungs will collapse satisfactorily only when the air is introduced at a pressure higher than the atmospheric pressure. This pressure, which is distributed through the whole pleural cavity, allows distention to occur at the weakest spot. This distention appears soon after filling. If filling is done in the pleural cavity where the retrosternal pouch overlaps the opposite side, distention appears rapidly. In typical cases the leaves of the mediastinal pleura are directed obliquely from front to back and from left to right; the left pouch projects beyond the right anteriorly. If the patient received insufflations into the left pleural cavity, the left pouch reacts to pressure by forcing it back, the distal end finds its way between the thoracic wall and the costal pleura of the opposite side, slips and, separating the costal pleura, projects into the contralateral half of the thorax. In a number of cases a positive pressure in the hernial sac was constantly found, as well as in the principal pleural cavity. Distention of the retrosternal pouch was found only in young patients aged from 18 to 31 years, their age favoring a flexible mediastinum. In these young patients the pleura is rarely the seat of pathologic disturbances, such as pachypleuritides and adhesions found in older patients. There is an anatomic predisposition of the sternomediastinal pleural leaves for the formation of a distention of the retrosternal pouch. Although this complication is usually harmless and does not hinder the course of the pneumothorax, it is necessary to know how to administer the injections in such a way as to reduce the hernial pouch or at least to arrest its progress.

*Old Tuberculin vs Tuberculin Protein* — J. B. Barnwell and H. Pollard (Am Rev Tuberc 30:482 (Oct.) 1934) state that Seibert's tuberculin protein (T. P. T.) can be incorporated in dry powder in minute amounts (0.001 mg.) in tablets of dry lactose, with an accuracy comparable to that obtained by the dilution of old tuberculin by quantitative chemical methods. The lactose alone produces no reaction in tuberculous patients. Among those reacting to either T. P. T. or old tuberculin, the proportion of severe and mild reactions is about the same when roughly comparable protein doses are used. Seibert's tuberculin protein, 0.0001 mg., is equivalent in potency to 0.1 c.c. of 1:10,000 old tuberculin in terms of percentage reactions among students. Every student reacting to 0.0001 mg. of T. P. T. reacted to old tuberculin in some dilution up to 1:100.

Every patient with proved tuberculosis (about 100), including skin tuberculosis, reacted to some dose of T. P. T. up to 1 mg. As the doses of old tuberculin and T. P. T. are increased in multiples of 10, many more students react to T. P. T. than to old tuberculin. Twelve persons who reacted to T. P. T. and not to old tuberculin presented evidence of previous tuberculous infection in the x-ray pictures. One with such evidence gave a reaction to old tuberculin but not to T. P. T., and 7 were negative to both tuberculins (T. P. T. 0.01 mg. and old tuberculin 1:100). Sensitization does not account for the differences in the number of reactions between old tuberculin and T. P. T. The comparison of the proportion of reactors in simultaneous tests on apparently healthy persons is a delicate method of standardization of an unknown against a known tuberculin. Seibert's tuberculin protein in the doses used suggests that tuberculinization is at a higher level than that indicated by old tuberculin 1:100.

*Plaster-of-Paris Cast Jacket*—L. Girones (Arch. de med. cir. y especialid. 37.846 (Aug. 4) 1934) obtained a partial immobilization of the left side of the thorax of a tuberculous patient by means of a plaster-of-Paris cast provided with a large window over the healthy side. The patient had a history of a previous inflammatory condition and pulmonary adhesions accompanied by hemoptysis and severe diarrhea. X-ray examination demonstrated a cavity, 6 x 3.8 cm., in the left upper lobe below the clavicle. The right lung appeared normal. The patient's condition did not improve during the first weeks of observation. The expectoration increased to 55 c.c., while the erythrocyte sedimentation speed was high. Another x-ray examination showed the cavity to have increased by 6.8 x 4.5 cm. A plaster-of-Paris cast was placed over the thorax and after 2 days a large window was cut on the right side. At the end of a month the expectoration was reduced to half its former amount and the erythrocyte sedimentation speed to 31, while the weight had increased 4½ pounds (2 kg.). The cavity was reduced to 5.2 x 3 cm. and the left half of the thorax had retracted considerably. The pulmonary tissue in the region of the anterior aspect of the second rib showed marked retraction on the x-ray picture. Another cast was applied at a later date. The therapeutic result was satisfactory and warrants further application of casts to patients having unilateral and bilateral cavities in which pleural adhesions make pneumothorax impossible.

*A-O, Preparation of*—A specific vaccine for tuberculosis was prepared, studied, and experimented with by R. Arima, K. Aoyama, and J. Ohnawa (Arima's Institute for Experimental Medicine, Osaka, Japan, 1931). It is prepared with tubercle bacilli of human type and possesses the following specific characteristics: It can be absorbed with ease in an organism, the protoplasm of the tubercle bacilli is preserved in its natural condition; the bacilli are sterile and nonpathogenic; they are from such stems of bacilli as possess the strongest immunizing powers; and the antigen unit or the proportional strength of the immunizing powers of the vaccine is exactly measured beforehand by a specific method.

Saponin extracted out of the skin of soapberries (*sapindus mukuroji japonica*) added to the culture medium has been found to be effective in depriving the bacilli of the main proportion of the waxy substance, or, in other words, of the

acid-fast quality. The additional use of lipase may be made when the removal of the substance is found insufficient.

The tubercle bacilli thus treated may be applied to living organisms with an assurance of safety and efficaciousness, for the bacilli are capable of being dissolved with ease by the body fluids and their faculty of provoking the immunizing function in an organism is unrestricted and gives rise to no local disturbance.

It usually takes a period of 3 to 4 years to reduce ordinary tubercle bacilli into a state of sterility, even when placed in saline solution and kept in a refrigerator. However, only 1 to 1½ years' time is sufficient to bring bacilli denuded of waxy substance through the use of saponin and lipase into a similar state. The sterility has been proved both by animal and cultural experiments. A-O contains, besides sterile bacilli in physiological saline solution, 0.5 per cent carbolic acid, in conformity with the regulations of the Japanese Government in force regarding bacilliary preparations. The acid in this proportion does no damage to the natural condition of the protoplasm and, therefore, to its innate powers of exciting specific immunity in an organism.

A-O must be kept in a dark cool place. It keeps in perfect efficaciousness until the date stamped upon the cover of the package.

*A-O Prophylaxis*—R. Arima, K. Aoyama, and J. Ohnawa (The Arima Kenkyusho, Osaka, Japan, 1931) state that there are two practical uses for A-O, *viz.*, prophylactic and therapeutic. As a pre-infection prophylactic measure, A-O may be given to all newborn babies and infants, who thus will be made tuberculosis-proof. Two instances of this are cited.

Ikujū, of the Osaka Municipal Nursery, gave prophylactic treatment of A-O to 69 newborn babies and infants during a period of 6 months, February to July, 1929. An investigation was made June, 1930, and the findings were as follows: (1) In no single case did the treatment prove harmful in any respect, (2) no deaths took place among the recipients of the vaccine, (3) not one case of tuberculosis developed among the 69 infants, despite the fact that 22 infants out of the 69 had shown a positive dermal reaction to tuberculin before the A-O treatment was given and that all of them belonged to the lowest classes of society and lived in poverty and unsanitary surroundings.

Buschmann, of Bielefeld, Germany, reported that A-O injections given to newborn babies were not only harmless, but effective in making them tuberculosis-proof. He gave A-O injections to 87 newborn babies of tuberculous parents from May 1, 1928, to March 1, 1929, and an investigation made in July, 1930, *i. e.*, 16 to 26 months after the injections were given, showed that there had been no deaths among this group. An exception was the case of a baby who developed tuberculosis in the knee joint 22 months after the injection, but who subsequently was cured by A-O treatment.

The first year, injections of A-O are given for the purpose of arousing and developing immunity. A-O No. 2 is used every month or twice monthly until a course of 5 injections is completed, thus completing the course. The interval that must elapse between injections may be adjusted so as to suit the circumstances and convenience, but it is advisable that it should not be shorter than 2 weeks or longer than 1 month.

During the second year, A-O injections are given to further develop and strengthen the immunity already produced by the first year's injections. These may be begun with A-O No. 3 about 1 year after the first injection of the first

course took place, to be repeated every 4 months until a course of 3 injections is completed.

Another prophylactic application of A-O may be called *therapeutic-prophylactic vaccination*. A-O treatment of this description is being given in Japan, with invariably good results, not only to primary school pupils, but to students of middle schools, girls' higher schools, normal schools, the inmates of nurseries, factory hands of both sexes, and others. The results have been so satisfactory that the vaccination has become practically nation-wide in Japan. The treatment has been found effective in relieving both subjective and objective disturbances, such as habitual coryza, night-coughs, night-sweats, lymphoma, oligohypomenorrhea, etc., and in improving appetite, nutrition, complexion, general health and feelings, accompanied at the same time with an improvement in the x-ray picture.

*A-O Treatment.*—The therapeutic use of A-O was first applied to humans in 1919, the subjects being 4 physicians, provedly and suspectedly tuberculous. The experiment showed that the vaccine was not only harmless, but noticeably efficacious. It was, therefore, prescribed for increasing numbers of tuberculous patients, and by the spring of 1927, the number of persons who had taken it prophylactically and therapeutically totaled about 20,000. In the meantime, the Japanese Government authorized the sale of the vaccine and the preparation was first placed upon the market in April, 1927. About 230,000 persons took the vaccine from that date up to the end of 1930 and it continues to be in ever-increasing demand.

In the therapeutic treatment of humans, A-O is given in the proportion of 1 AE per kg. of the corporal body weight. In case of prophylactic vaccination, however, 2 AE and 3 AE may be used. One c c of A-O No. 1 contains 50 AE (Antigen-Einheit) (or 25,000 bacilli approx); A-O No. 2, 100 AE (or 50,000 bacilli approx), and No. 3, 150 AE (or 75,000 bacilli approx).

It is highly important that the exact *indications* should be observed, for they are the indices to the powers of reaction which a particular patient may possess. A-O is an agent which calls forth or increases, through biological reaction of its own, the immunizing powers in a subject. It follows, therefore, that the earlier the stage of the disease and the less serious the affliction, the more effective the injection. Cases of purely surgical tuberculosis, ophthalmological tuberculosis, glandular conditions, etc., are the cases where the efficaciousness of A-O is most conspicuous. In these cases it has often been observed that only 1 or 2 injections have caused a longstanding inflammation to improve and repeated injections have brought about perfect healing in a comparatively short time.

General treatment must not be neglected when A-O injections are being given. Great care should be taken to secure good nutrition for the patient.

In severe cases of tuberculosis, however, general symptomatic treatment should be mainly relied on, A-O being used only supplementary.

A-O injections are strictly hypodermic and may be given either in the upper arms, between scapulæ, or in the thighs. The vaccine is classified into No. 1, No. 2 and No. 3, to suit the use to which it is put. For therapeutic purposes, No. 1 alone is used, with an interval of 1 week to 10 days, while for prophylactic purposes, No. 2 and No. 3 are employed.

The *interval* between injections may be extended 1 or 2 days or even more, in case of an abrupt change in the general condition of the patient, or any other circumstances that may hinder the prescribed course of injections, but under no condition should the intervals between injections be cut shorter than above mentioned.

It is interesting to note that in exceptional cases where A-O injections, carried out at prescribed intervals, failed to produce the normal results, wonderful results were achieved when the intervals between injections were greatly extended.

The prescribed *dose* of A-O is 1.0 c.c. to 50 kg of corporal weight. For instance, 0.8 c.c. is to be given to a patient with 40 kg of weight, 0.5 c.c. to one with 25 kg; 0.2 c.c. to a child of 10 kg, etc. (For a dose of less than 0.5 c.c. it is convenient to employ A-O For Juvenile Use) The dose may not be increased, but remains at 1.0 c.c. for a person with more than 50 kg. of corporal weight.

The first course consists of 15 to 20 injections or more, carried out in accordance with the directions, the variations in the required number of injections being governed by the difference in the degree of the progress of the disease, the constitution of the patient, and the readiness of the patient's response to the injections. Following the course of treatment, an observation period of from 3 to 6 months should elapse, to observe the effect of the injections. A second course of 6 to 10 injections or more may be given, in case it is felt advisable. There is no limit to the number of injections, they may be given as many times as required. The injections of the second course are given in accordance with the rules governing the first course, *viz.*, No. 1 alone is employed with the prescribed intervals.

In case *additional injections* are found advisable after the completion of the second course, they may be taken up with either No. 1 or No. 2, at the rate of once a month at most, after 3 to 6 months from the final injection of the second course. For those who have recovered normal health and yet may feel uneasy and be desirous of taking supplementary injections as a precautionary measure, the injections of A-O No. 1 or No. 2 (the dose to be reduced proportionally to the corporal weight) every 2 to 4 months, may be prescribed. Through this means, the patient will be able to secure excellent continuity of the healing effect of A-O.

Since A-O is a strictly specific vaccine, it may not be used collaterally with other specific therapeutic agents, such as tuberculin, preparations made from tuberculin bacilli, or irritating protein therapeutics. In case A-O injections are instituted after using any one of the above mentioned therapeutic methods, a period of at least 1 week must elapse. The reason for this is that A-O is in a manner an irritating vaccine and its use with other irritating agents may mean too heavy a burden upon the affected organism. General therapeutic measures, symptomatic and pharmaceutic treatment, especially the injection of calcium, however, may be employed together with A-O injections. These do not interfere with the action of the latter, but have been found to aid it in producing an ideal result.



*Contraindication.*—The only contraindication in which A-O may not be used is *massive hemoptysis*. In cases of hemoptysis, such as blood stripes in sputum or bloody sputum, A-O is not only uninjurious, but has often caused the hemorrhage to stop. In the latter cases A-O must be prescribed in a smaller dosage, and physical rest and strict observance of general hygienic laws should be ordered.

*Treatment of Tuberculous Empyema.*—J. Rosenblatt (J. Thoracic Surg 3:422 (Apr) 1934) presents the end-results in a series of 21 cases of toxic tuberculous empyema treated conservatively and followed up for from 3½ to 11 years. The principles underlying the treatment depend on the number of complicating factors present. The therapeutic measures commonly employed in tuberculous empyema may be classified as conservative and radical. The conservative measures frequently used are: Aspiration, aspiration and air replacement, aspiration and irrigation with antiseptic solutions, such as sodium chloride, gentian violet, acriflavine and potassium permanganate, and oleothorax with a 5 to 10 per cent solution of aromatized oil. The treatment in the 21 cases reported consisted of **aspiration of as much of the pus as possible, replacing it with air**, and the injection of from 2 to 3 cc (½ to ¾ dram) of a **saturated alcoholic solution of methylene blue** just before the needle was withdrawn. This treatment was repeated at varying intervals, depending on the rapidity with which the fluid reaccumulated. The amount of air introduced was dependent on the amount of fluid aspirated and the intrapleural pressure. In large effusions with a free pleural cavity, a slightly negative pressure was left at the end of the treatment. If the pleural cavity became limited and further collapse of the lung was desired, enough air was introduced to produce a slightly positive pressure. This procedure was repeated periodically, as long as there was any fluid that could be aspirated, though the intervals between treatments could be gradually increased as the reaccumulation of the pus became slower. The successful cases remained under treatment for from 8 months to 4 years. The average length of treatment was approximately 2 years. Eleven patients were cured and 10 died. Of the cured patients, 10 are entirely free of symptoms and are able to work, and 1 is under treatment with pneumothorax for a newly-developed lesion on the opposite side, but the empyema has entirely cleared up and the lung reexpanded. Among the patients who recovered, 2 developed empyema as a result of perforation of the lung, and of these two, 1 had also a fair-sized bronchopleural fistula. One patient with a small draining sinus in the chest wall and a small intermittently patent bronchopleural fistula also recovered. In this case the sinus persisted for about 2 years and has been healed for the past 3 years. Of the patients who died, 4 showed considerable improvement temporarily, and the ultimate fatal outcome was due to the progressive pulmonary disease. Six failed to show improvement. The empyema was probably an important factor in the unfavorable outcome of 3 cases. In two of these, large bronchopleural fistulas were present.



# Syphilology

*by*

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**SYPHILIS.**—Since the turn of the century there has been an immense increase in knowledge concerning syphilis. In the past three decades the causative organism has been discovered, the Wassermann and precipitation tests devised and perfected, and there has been such an increase in therapeutic drugs and methods as to entirely revolutionize previous ideas as to prognosis and curability. While the past year has witnessed no remarkable discoveries, a search of the voluminous literature reveals new and interesting facts regarding the history of syphilis, and various other aspects of the disease including therapy.

**HISTORY.**—It is a curious fact that while such enormous strides were being made in knowledge of the causative, diagnostic and therapeutic aspects of syphilis since 1900, the legend concerning the American origin of the disease received added support in several texts. According to recent exhaustive studies by R C Holcomb (U. S. Nav. M. Bull. 32:4, 1934), this view is inconsistent and anachronistic when the evidence is reviewed. For more than a third of a century after the discovery of America there was no mention of Columbus in the texts in connection with the origin of syphilis. It followed the introduction of a remedy, holy wood or guaiacum, that for 2 centuries held sway as a specific for syphilis. This wood came from America, and about a decade after its introduction into Europe there appeared the early signs of associating the disease with the first voyage of Columbus. Holcomb has unearthed evidence that the disease was already widespread throughout Europe as early as March 25, 1493. Inasmuch as Columbus and his sailors returned from their first voyage to the Americas on March 15, 1493, it would have been impossible for the survivors of his voyage to have spread the disease extensively in so short a time. Holcomb attributes the lack of definite knowledge of the disease previous to 1493 to the slow development of the art of printing, and the confused state of ancient dermatology, particularly as regards nomenclature.

**PUBLIC HEALTH ADMINISTRATION.**—The next public health movement should be directed towards the control of venereal diseases. This is the opinion voiced by E C Fox (Texas State J. Med. 29:577 (Jan.) 1934), who urges the enlistment of the entire medical profession in the campaign. He recommends that in every case of syphilis the source of the infection, other contacts of the source, and the contacts of the patient should be investigated, and feels that otherwise there will be an increase in the prevalence of syphilis as the untreated and inadequately treated will spread the disease the same as any other communicable disease. R A Vonderlehr (Virginia M. Monthly 60:309 (Aug.) 1933), in 1933, had likewise urged the cooperation of physicians, local health authorities and responsible citizens in fighting the spread of syphilis. The physician should interest himself in the education of patients in fundamentals of sex hygiene and the danger of neglecting infections, and in the instruction of promiscuous persons in the methods of prophylaxis. It is his duty to keep informed on modern methods of diagnosis and treatment and to support government work in control of syphilis as well as other venereal diseases. The need for free treatment for patients unable to pay is of the greatest importance. A Kissmeyer (Bull. Soc. franç. de dermat. et syph. 40:926 (July) 1933) points out

that in Denmark, where free treatment began with the law of July 2, 1790, syphilis has almost disappeared.

**CLINICAL CONSIDERATIONS AND PATHOLOGY.**—*Cardiovascular Syphilis.*—"All physicians know that syphilis heads one of the three great etiologic groups of cardiovascular disease" is the statement of L. A. Conner (J. A. M. A. 102:577 (Feb 24) 1934) in a comprehensive article on "The development of knowledge concerning the rôle of syphilis in cardiovascular disease." They know that it accounts for from one-sixth to one-fourth of the deaths from this disease among adults. And, finally, they know that at the present time the syphilitic group is the only one of the three great classes for which preventive measures are known and are available. Are they doing everything possible to prevent these grave consequences of syphilis?

Pathologists and clinicians have always disagreed about the frequency of syphilitic heart disease apart from changes resulting from aortitis. Clinicians have considered cardiac syphilis as not uncommon, while pathologists generally have insisted on its comparative rarity. It can only be concluded that if the lesions of late acquired syphilis are common in the myocardium, they exist in forms which render them indistinguishable from those due to other and more probable causes. It seems safe to say, from evidence on hand, that syphilis is rarely a cause of coronary disease, except as it involves the proximal portion of those vessels as a part of the process of aortitis. Most of the reported cases of syphilitic disease of the pericardium and endocardium have not withstood critical investigation. If the frequent cases are excluded in which involvement of the aortic cusps is the direct extension of a syphilitic process in the aorta and the rare instances of disease of the pulmonary valve as a part of a similar process in the pulmonary artery, only a few well authenticated examples of syphilitic valvular disease remain.

J. von Fernbach (Ztschr. f. klin. Med. 125:453, 1933) states that syphilitic myocarditis and aortitis generally do not occur until years or decades after the infection, but it is questionable if the spirochetes remain latent all this time. His studies of a number of out-patients with syphilis indicated that the heart may be affected in the secondary stage, and in view of this emphasizes the necessity for thorough treatment in all early cases of syphilis.

**Syphilitic Jaundice.**—Perhaps no syphilologist has made as thorough a study of syphilitic jaundice as Milian, and a recent paper on this subject by G. Milian (Bruxelles-med. 14:523 (Feb 18) 1934), while in general a rehash of his previously expressed views, may be worth a brief review. Syphilitic hepatitis may take the form of catarrhal icterus, which usually remains unrecognized, since it is not accompanied by any other syphilitic symptoms. Clinically, this jaundice resembles the jaundice of secondary syphilis which sometimes follows the roseola. It runs a mild course and disappears in 3 or 4 weeks even in the absence of anti-syphilitic therapy.

Wherever icterus is an isolated phenomenon, syphilis should be thought of and the patient examined for other signs of this disease. Since icterus usually appears in the secondary or secondary-tertiary period, signs usually present at this stage should be looked for. Frequently there will be an accompanying head-

ache. The temperature is moderately elevated. Enlarged lymph glands should be sought. Digestive disturbances are lacking. A Wassermann test should always be made.

Catarrhal icterus of the infectious or gastrointestinal type can be easily eliminated, since it is almost always accompanied by a high fever and by digestive disturbances as vomiting and diarrhea.

Icterohemorrhagic spirochetosis and various forms of acute infectious jaundice are easily distinguishable, having each its own symptomatology. Only malarial jaundice closely resembles the syphilitic type, but differentiation should be easy by means of laboratory examinations or therapeutic tests.

Milian regards posttherapeutic icterus as a manifestation of syphilis—a mono-recurrence. This view is not generally accepted. His recommendations that arsenicals are better avoided until at least a month's treatment with a slow-acting drug, as mercury, is somewhat different from his own expressed views of several years ago that icterus is most apt to occur in cases in which small or insufficient doses of an arsenical are used.

U J Wile and W. M. Sams (Am. J. M. Sc. 187: 297 (Mar ) 1934) believe, contrary to Milian's views, that posttherapeutic jaundice cannot be regarded as a hepatic recurrence. In a series of 10,021 cases of syphilis, the diagnosis of syphilis of the liver was made clinically, following operation, or at autopsy in 91 cases, or 0.9 per cent. Their studies indicated a possible relationship between postarsphenamine jaundice and infectious jaundice.

**Gastric Disturbances Secondary to Syphilitic Infections.**— Syphilis plays an important rôle in the production of gastric symptoms, according to J. Friedenwald and S. Morrison (Am. J. Syph. and Neurol. 18: 163 (Apr ) 1934). These gastric manifestations may occur as a result of syphilitic lesions of the stomach itself or may be produced secondarily due to a generalized systemic infection or to syphilitic involvement of one or many organs. Gastric syphilis is far more frequent than was formerly recognized, due to the fact that diagnostic criteria of this affection have been somewhat modified as a result of increasing experience. The authors state that the stomach may be secondarily involved (1) as a result of the general syphilitic infection, or (2) as the result of syphilitic disease of special organs.

The *gastric symptoms* occurring in early syphilis are nausea, vomiting, eructations, fullness, distention, abdominal discomfort, and vertigo. Whether such manifestations are actually due to syphilitic involvement of the stomach or are vagotonic in origin has not been determined. There may be no other evidence of syphilis except a positive Wassermann reaction.

The secondary gastric symptoms occurring in advanced syphilis may be due to syphilitic lesions involving various organs or systems or may be produced as the result of a purely generalized infection. Cases may resemble gastric ulcer, gastritis with achlorhydria, scirrhus carcinoma; may show gastric retention or present functional disturbances of the stomach as in gastric crises.

Attention is called to the fact that *gastric ulcer* and *tuberculous crises* are not uncommonly associated in the same patient. The ulcer is not of syphilitic origin.

in these cases, as organic syphilitic affections of the stomach are not known to occur in association with neurosyphilis.

Five clinical forms of gastric crises are recognized :

- 1 Mild types accompanied by slight pain, little vomiting but excessive esophageic explosions
- 2 Abortive types with mild attacks of pain and vomiting of short duration
- 3 Severe types with extreme pain and excessive vomiting
- 4 Irregular types with almost daily crises
- 5 Complicated types with complications such as gastric hemorrhages large in quantity, and periodic gastric hypersecretion associated with pylorospasm.

*Gastric neuroses* may be associated with syphilitic infections, manifesting themselves with symptoms of hyperchlorhydria, hypochlorhydria, cardiospasm, pylorospasm, bulimia, aerophagy, gastralgia, regurgitation, and vomiting

Prompt and complete restoration to health and disappearance of gastric symptoms as a result of antisymphilitic treatment is at least important positive evidence in demonstrating the correctness of the diagnosis. In suspicious cases a Wassermann test of the blood should always be made

**Reinfection in Syphilis and Chancre Redux.**—Persons who have been infected with syphilis are later liable to develop at the former site of the chancre an indurated lesion, the interpretation of which is difficult. The monorecidive is a recurrence of the chancre *in situ*. It occurs within 2 years, occasionally as late as 7 years after the cessation of treatment. It is an indurated lesion which contains spirochetes and occurs at the site of the original chancre. It is accompanied by enlargement of the regional lymph glands from which spirochetes can often be obtained on aspiration. Since it is a relapse of syphilis, the patient has a positive blood Wassermann reaction at the time the monorecidive appears. J. V. Klauder and T. Butterworth (Am J Syph and Neurol 18:433 (Oct) 1934) call attention to the difficulty of differentiating such a lesion from the chancre of reinfection. Reinfection implies a proved previous attack of syphilis, adequately treated, and serologically and clinically cured. The chancre of the second infection must follow exposure and is often less indurated than the average chancre of a primary infection. Ideally it contains many spirochetes and is accompanied by a satellite adenopathy. When a chancre of a reinfection first appears, the blood Wassermann reaction of the patient is negative, but later becomes positive. If the patient is untreated a secondary rash appears.

The "chancre redux" is a gummatous nonerosive papule occurring at the site of the chancre and is differentiated from the monorecidive and the chancre of reinfection by the absence of a positive darkfield and satellite adenopathy. The blood Wassermann is usually positive and histologic examination reveals gummatous structure.

K. Schreiner (Arch f Dermat u Syph 169:397, 1933) attributed the development of chancre redux to a changed biologic reaction of the organism to the spirochete. This reaction, as shown by the luotest and many of the clinical symptoms, resembles the reaction of tertiary syphilis.

**Asymptomatic Neurosyphilis.**—Asymptomatic neurosyphilis is the most important type of neurosyphilis, according to P. A. O'Leary (Proc Staff Meet



Mayo Clin. 9:756, 1934) The reasons for this inclusive statement are: (1) Asymptomatic neurosyphilis is the forerunner of clinical neurosyphilis. (2) In the great majority of cases, adequate and intensive treatment successfully controls asymptomatic neurosyphilis (3) In view of the fact that this form of the disease responds so well to treatment, its early recognition and adequate treatment are essential in the prevention of clinical neurosyphilis (4) In no other form of the disease is the need for individualization of treatment rather than systematization of treatment better demonstrated.

The only means by which asymptomatic neurosyphilis may be recognized is by the examination of the spinal fluid O'Leary divides asymptomatic neurosyphilis into an *early* and a *late type*. The early form includes those cases in which the disease is of more than 4 years' duration and in this type there is a tendency for the neurosyphilis to increase The early type responds to treatment more satisfactorily than the late type. O'Leary strongly recommends fever therapy

**LABORATORY METHODS.—Sensitization of Wassermann Reaction.**—Various methods of increasing the sensitiveness of the Wassermann reaction so that it will be positive in all cases of syphilis have been tried Unfortunately, there is a tendency when the sensitiveness of the test is increased for it to give nonspecific results H T Schreus and R. Foerster (Ztschr. f. Immunitätsforsch u exper Therap 82 53, 1934) propose a specific method of increasing the sensitiveness of the reaction by adding a subthreshold amount of a known positive serum to the serum to be examined, thus bringing the amount of antibody contained in it up to an amount that will be demonstrated by the test The amount of antibody added must be small enough not to produce a positive reaction by itself

Sensitization of antigens for the Wassermann reaction with cholesterol, sitosterol, and other sterols bears an important relationship to the kind of primary incubation and amount of complement employed J A Kolmer, C E Richter and E M Yagle (Am J Syph and Neurol 18:204 (Apr ) 1934) found that with a primary incubation of 15 hours at 6° C, followed by 10 minutes in a water bath at 37° C, antigens sensitized with more than 0.2 per cent cholesterol or other sterols tend to yield falsely positive reactions with nonsyphilitic sera in the Kolmer modification of the Wassermann reaction

In the *Kolmer modification* of the Wassermann test, employing a primary incubation of 15 hours at 6° C, followed by 10 minutes in a water bath at 37° C, the reactions were more sensitive and specific with antigen reinforced with 0.2 per cent cholesterol, and used in doses of 10 units than in tests conducted with 0.4 per cent cholesterolized antigen and a primary incubation of 4 hours at 6° C, followed by 1 hour at 37° C

The Kolmer antigen sensitized with 0.2 per cent cholesterol gave best results in doses of 10 units The authors state that there is no advantage in sensitizing antigen with cholesterol just before use

In an investigation in which more than 20,000 tests were done and more than 30 techniques and methods were used, J. E. Nicole and E. J. Fitzgerald (Lancet 1 623 (Mar 24) 1934) found the Kahn to be the only specific test,

the Wassermann giving 0.7 per cent. false positives and some of the Meinicke tests as high as 3 and 4 per cent. false positives.

**TREATMENT.**—The physician of today who is called upon to treat syphilis in any of its stages may regard himself as most fortunate in comparison with the practitioner in the first decade of this century. The following table (C. S. Wright: *Ohio State M. J.* 30:362 (June) 1934) illustrates the therapeutic drugs and methods of today compared with those of 1908.

THERAPY OF SYPHILIS.	
In 1934	In 1908
ARSENOBENZENES	
Arsphenamine	
Neoarsphenamine	
Sulpharsphenamine	
Acetarsone	
(Stovarsol Spirocid)	
Tryparsamide	
BISMUTH	
MERCURY	MERCURY
FEVER THERAPY	IODIDES

The rapid introduction of new drugs and therapeutic methods since the turn of the century has resulted in considerable confusion as to the best methods of application. It is obviously impossible to standardize the treatment of syphilis in general, as late syphilis in particular requires individualization of therapy. However, standardization of treatment for early syphilis has always appeared feasible, due to the clear definition of the aims possible at the early stages of the disease, the youth and relatively good health of the patients, and their freedom from the intrinsic damage in later life produced by years of syphilitic infection. Therefore, the presentation of a uniform type of procedure in the treatment of early syphilis as a result of a massive investigation of worldwide scope is of paramount interest. Sponsored by the League of Nations Health Organization and carried through in the United States by the combined efforts of the U. S. Public Health Service and a group of 5 university clinics, J. H. Stokes, H. N. Cole, J. E. Moore, P. A. O'Leary, U. J. Wile, Thomas Parran, R. A. Vonderlehr and L. J. Usilton (*J. A. M. A.* 102:1267 (Apr. 21) 1934) present a résumé of modern principles. As a basis for a definition of the aims and methods of modern effective treatment for early syphilis, the records of 75,000 cases of syphilis were reviewed, of which 3244 were examples of early syphilis followed for 6 months or more, and 383 were followed for as long a period as 5 years or more.

The term "golden opportunity" applied by Pusey to the superior outlook of treatment begun in the primary stage of syphilis before the blood serologic tests become positive ("seronegative primary") has been justified abundantly by statistical analysis. The proportion of "cures" when treatment is begun in the seronegative primary stage is, as given, 71.4 per cent. average and from 83 to 86 per cent. best results. When, through failure of the patient to present himself or of his physician to diagnose primary syphilis until the blood test becomes positive, treatment is not begun until the so-called seropositive stage, "cure" is

attained in only 53.3 per cent. by average and from 64 to 70 per cent. by the best methods. This represents a clear loss of 18 per cent. in outlook for "cure" by the delay. If the patient goes on to the development of a secondary eruption, "cure" is attained in only 50 per cent. by average and 61 to 82 per cent. by best methods. Further statistics are given, but it is already apparent that early diagnosis and earliest possible application of treatment is the duty of the conscientious physician to his patient.

The Committee decided, after the study of considerable data, only part of which is abstracted here, that the modern system for the treatment of *early* syphilis must be continuous; it must employ an **arsphenamine** and a **bismuth** compound, the latter intramuscularly; it must call for not less than 20 and rarely more than 30 injections of the arsphenamine; and, in accordance with the principles generally recognized in the treatment of the disease, the system should call for continued treatment with heavy metal for 1 year after all symptoms and signs of the disease have disappeared. In order to determine this end point, blood tests should be taken at least at the beginning and end of each arsphenamine course and the patient should be warned of the lack of significance of the negative report from the standpoint of the schedule. Weak positives after a negative has appeared should be taken as seriously as strong or fully relapsing positives. A spinal fluid examination with Wassermann test, cell count, protein examination and colloidal gold test should be made before the end of the arsphenamine phase of treatment, or the introduction of any rest period. It is understood that such a system can be carried through only with adequate tolerance on the part of the patient, and this tolerance should be conserved in every possible way. The same system should be employed whether treatment is begun in the seronegative or seropositive primary or the secondary stage.

All standardization of treatment for early syphilis should be preceded by an examination of the urine for albumin, sugar and casts, and by a sufficiently detailed physical examination, to assure the absence of serious organic disease. Inquiry should be made as to symptoms of second and eighth nerve involvement, recent severe headaches, hepatitis and pregnancy before the first treatment is given.

The scheme of treatment for early syphilis as advised by the Committee\* was published in Ven. Dis. Inform. 10:53, 1929, and since has been copied into numerous papers and texts dealing with syphilis and its treatment. The more publicity this scheme of treatment receives among the medical profession the more quickly will all cases of syphilis be adequately treated.

**Arsphenamine.**—The majority of published papers on the arsphenamines during 1934 deal with reactions and methods of treating them. Thus, M. Scarf (J. A. M. A. 102:2159 (June 30) 1934) reports 6 cases of serious arsphenamine reactions including a case of aplastic anemia, 2 cases of hepatitis, a case of hemorrhagic encephalitis, a case of rupture of an aortic aneurism following neoarsphenamine therapy, and a case of transverse myelitis. Scarf points out that virtually all of these untoward reactions followed further administration of the

\* Readers are referred to the *CYCLOPEDIA OF MEDICINE*, Vol. XI, p. 1024, for a copy of this "Scheme of Treatment" in table form.

drug after warning symptoms of intolerance, and advises a careful evaluation of symptoms and signs as they appear in syphilitic patients under treatment with the arsphenamines

The *by-effects* of arsenobenzene therapy were studied in 1090 patients while receiving a total of 20,000 injections, by W. Burckhardt and E. Diem (Arch. f. Dermat. u. Syph. 170: 435, 1934). By-effects were observed in a total of 292 cases, or slightly over 25 per cent, this high percentage being due to the fact that the mildest cases of shock and transitory exanthem were reported. Acute shock occurred in 37 cases, protracted shock in 121, maculo-urticarial exanthem in 65, eczematoid-lichenoid exanthem in 81, purpura in 8, joint pains in 29, icterus in 39, and herpes zoster in 16. One case of purpura and 1 case of icterus ended fatally. The authors from their studies concluded that the majority of exanthems were allergic rather than toxic, they found very little difference in different preparations—arsphenamine, neoarsphenamine, neosilver-arsphenamine, etc.

This appears to be an unusually high incidence of reactions compared to statistics of reactions from various clinics in the United States, such as those of Marshall and others.

A fatal case of severe bone-marrow disease following intensive neoarsphenamine treatment is discussed by Bruni (Clin. med. ital. 65: 583 (June) (1934)). Ecchymoses developed on the limbs and later hemorrhages of the gums occurred. He warns, as many have done before, against the use of arsenicals in patients with a hemorrhagic diathesis.

In the article quoted previously (Stokes, Cole, Moore, *et al*, *loc. cit.*), *reaction prevention principles* were formulated as follows.

1. Inquire into the history of idiosyncrasy, allergic tendencies, skin irritability, focal and intercurrent infection, liver damage, and pregnancy before treatment is started.
2. Question the patient before each treatment regarding (a) itching or rash, (b) purpura and melena, (c) gastrointestinal reaction, (d) condition of the mouth and teeth.
3. Examine the eyes (jaundice), face (dermatitis), mouth (salivation, bismuth pigment, purpura), flexures of the elbows (dermatitis), wrists and ankles (purpura) before each treatment, take the temperature.
4. Make the first dose of the drug not more than half the full dose.
5. Pull back on syringe pistons before intravenous injection, to be sure of vein entry, before an intramuscular injection, to be certain a deep vessel has not been entered.
6. Inject intramuscularly into the inner angle of the upper outer quadrant of the buttock and massage long and well after the injection.
7. Inject all solutions for intravenous use slowly through a small needle, not faster than 0.1 Gm. (1½ grains) per minute for neoarsphenamine.
8. Keep carbohydrate and alcohol low in the diet, and protein and fat high.
9. Permit only a light meal before and after an arsenical, and prescribe a mild cathartic the morning after.
10. Make a urine examination biweekly.
11. Give calcium freely.

**DETERMINATION OF ARSPHENAMINE SENSITIZATION**—Certain types of post-arsphenamine dermatitis, notably the vesicular and exfoliative eruptions, are due to sensitization of the patient to the drug. Various types of skin tests—intradermal, scratch and patch—have been tried in an effort to determine which patients are sensitized, so that this danger of arsphenamine therapy might be avoided.

A. B. Cannon and M. B. Karelitz (Arch. Dermat. and Syph. 29: 485 (Apr.) 1934) performed intradermal tests on 243 patients of whom 209 were syphilitics. Their conclusions were that the experiments failed to show any constant relationship between the reactions to the intradermal test and the clinical reactions of these persons to arsphenamine therapy. The test is lacking in specificity and is of little or no diagnostic value.

The patch test was found by W. W. Robinson (South. M. J. 27: 845, 1934) to be of no practical value for the demonstration of arsphenamine sensitization, since it is sometimes positive in normal individuals and often negative in those known to be arsphenamine sensitive.

**TREATMENT OF POST-ARSPHENAMINE REACTIONS.**—**Sodium thiosulphate** for a number of years has been the popular remedy for the treatment of post-arsphenamine reactions, particularly dermatitis. L. W. Shaffer (Arch. Dermat. and Syph. 29: 173 (Feb.) 1934) states that much more can be done for post-arsphenamine dermatitis than to limit efforts to the use of sodium thiosulphate alone. The introduction of **calcium thiosulphate** was a step in this direction, but the amount of calcium so administered falls short of producing calcium saturation, which is desirable. Shaffer recommends that 1 Gm. (15 grains) of **sodium thiosulphate** and 50 c.c. ( $1\frac{2}{3}$  ounces) of a 50 per cent. solution of **dextrose** be injected intravenously daily for from 3 to 5 days. The administration of the dextrose should be followed in  $\frac{1}{2}$  hour by 5 units of **insulin**. Using this method he has been able to shorten the time of hospitalization to an average of 8 days.

In 5 cases of *jaundice* which developed during treatment of syphilis with neoarsphenamine, B. Appel (Arch. Dermat. and Syph. 27: 401 (Mar.) 1933) treated the patients with intravenous injections of **sodium dehydrocholate**. There was a prompt fall of the icteric index and rapid recovery.

K. Fulst and M. Fellner (Deutsche med. Wchnschr. 59: 1856 (Dec. 15) 1933) recommend the use of **liver extracts** in the treatment of arsphenamine toxicoses on the basis that a dysfunction of the liver is the causal factor. Every second day the patient receives an injection into the gluteal muscle beginning with 2 c.c. ( $\frac{1}{2}$  dram) and increasing gradually to 5 c.c. ( $1\frac{1}{4}$  drams). For the prevention of arsphenamine intolerance, U. Rebaudi (Ann. d. mal. vén. 29: 481, 1934) uses a **liver amino-acid** prepared by himself. Two or 3 c.c. ( $\frac{1}{2}$  to  $\frac{3}{4}$  drams) of this are aspirated into the flask containing neoarsphenamine and stirred until the powder is completely dissolved. The injections are very slowly given intravenously. The author believes it thus possible to give intensive treatment, which is generally believed best for early syphilis.

**Iodides, Status of.**—The iodides are not spirocheticidal and have no influence on the serum reactions of syphilis. Thus, S. S. Greenbaum and J. Cobane (Am. J. Syph. and Neurol. 18: 289 (July) 1934) believe that they have no place in the treatment of early syphilis, with the possible exception of certain cases in which the arsenicals and heavy metals might be contraindicated, but even in these, the administration of small doses of the least toxic forms of heavy metal would give better results than could ever be obtained with iodides. The theory that in chronic syphilis, the iodides dissolve fibrous tissue, thereby allow-

ing spirocheticidal remedies to reach the organisms, is hardly tenable. There is good reason to believe that in a complete replacement fibrosis the spirochete is actually destroyed. The authors believe that much better results can be obtained with the arsenic and bismuth compounds.

**Vaccine Therapy of Early Syphilis.**—After years of experimentation, Hilgermann (E. Neuber: *Dermat Wchnschr* 98:229 (Feb 24) 1934) produced avirulent spirochetes adapted for active immunization. This spirochete vaccine was used in 215 cases, including 28 cases of early syphilis, 129 of secondary syphilis, 25 of tertiary cutaneous syphilis, 21 seropositive latent cases, 7 cases of congenital syphilis, and 5 of mixed ulcer. In the early cases the spirochete findings were not affected by 3 injections of the vaccine given over a period of 6 weeks. The clinical manifestations of tertiary lues were rapidly affected. Secondary manifestations were unaffected. The author concluded that while vaccine therapy alone is insufficient to free the body of spirochetes, it has a field of usefulness in cases in which normal production of antibodies is decreased, as in old latent or malignant cases, and may prove a valuable aid to chemotherapy.

**Adjuvant Remedies.**—In addition to specific antisyphilitic remedies, A. Galliot (*J de méd de Paris* 54:14 (Jan) 1934) recommends other forms of treatment, on the ground that the patient must be considered as well as the microorganism. The purpose of these adjuvant remedies is to improve the assimilation of the antisyphilitic drugs and to make their action more intense and lasting, and to improve the general condition of the body, so as to make it more capable of resisting spirochetes. Galliot recommends such measures as **bland diet, hygiene of the mouth and teeth, good general hygiene, a quiet life, and avoidance of alcohol and sexual indulgence.** Treatment at **mineral springs** is useful, as **sulphur waters** help in the elimination of mercury and bismuth. If rest periods are desirable, **Zittman's decoction** is recommended as a valuable preparation during such periods.

**Treatment of Congenital Syphilis.**—Chief interest in the therapy of congenital syphilis has centered on the value of **acetarstone** (stovarsol, spirocid). This drug was first synthesized by Ehrlich in 1909 while searching for his ideal spirocheticide. He designated it as 594. Levaditi and Navarro-Martín later showed that acetarsone absorbed from the stomach was less toxic than when absorbed after injection.

Among the reports on the use of acetarsone by mouth during the past year is that of B. M. Joseph (*J. M. Soc. New Jersey* 31:343 (June) 1934), who treated 14 cases with a combination of **acetarstone** by mouth and **bismuth** intramuscularly. His results were good but the conjoint use of bismuth confuses his results. J. F. Coppelino (*Am. J. Dis. Child* 48:272 (Aug) 1934) treated 20 syphilitic infants, giving 0.005 Gm ( $\frac{1}{12}$  grain) of **acetarstone** per kilo ( $2\frac{1}{2}$  lbs) of body weight daily for the first week, 0.01 Gm ( $\frac{1}{6}$  grain) for the second week, 0.015 Gm ( $\frac{1}{4}$  grain) for the third week, and 0.02 Gm ( $\frac{1}{3}$  grain) for the following 6 weeks. It was his opinion that the results of therapy equalled those obtained with bismuth and he concluded that acetarsone is the drug of choice for syphilitic infants, but it is not so efficacious in the treatment of older children. F. Eckardt (*Jahrb. f. Kinderh.* 141:278, 1934) recommends acetar-

sone in the treatment of congenital syphilis because it can be given orally and because of the high percentage of good results. C. F. Friedman (Am. J. Dis. Child 48 548 (Sept ) 1934) found that infants of from 3 weeks to 4 months of age all showed clinical, serologic, and roentgenologic cure. By the latter is meant the prompt healing of syphilitic lesions of the bone as demonstrated by the x-rays. The reviewer has had virtually the same experience with acetarsone. In children under 1 year of age it works magically, but it must be recalled that a single injection of bismuth or a short course of mercury rubs will also work magically in syphilis of very young infants, but its action is by no means as magical in older cases of congenital syphilis. For children over 1 year it is recommended as an adjunct to bismuth therapy or for administration during rest periods from injection therapy.





# **Diseases of Teeth and Gums**

*by*

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**DENTAL CARIES.—Etiology.**—There is no agreement as to the etiology of dental caries. A comprehensive account of the subject of active investigation, discussion and controversy of the causative factors of dental caries is presented by Theodore Rosebury (*Dental Cosmos* 76: 771 (July) 1934).

The term "dental caries" refers typically to a condition that is prevalent among children, adolescents, and young adults, occurring in the pits and fissures of the crowns of the teeth and at their points of contact. There are other varieties of dental caries, but the writer singles out this variety because it represents a clearly defined clinical and pathological entity and it constitutes a public health problem more important than the total of all other varieties of dental disintegration in man. This form of dental caries always begins in the enamel; it occurs in regions on the surfaces of the teeth which are generally food-retentive, and which are difficult to keep clean. It is observed in individuals who are apparently enjoying normal health. It is known to have increased with advancing civilization. The condition clearly begins at the surface of the tooth and progresses inward toward the pulp, and its manner of localization in the so-called "non-selfcleansing" regions of the tooth surface is striking and consistent. Dental caries is unique among diseases, it has no parallel elsewhere in the body. This type of injury produces no inflammatory response, there are no cells in either dentine or enamel, and hence these tissues manifest no cellular reaction. Susceptibility to dental caries is essentially a question of susceptibility of the enamel. This tissue, because it is almost entirely composed of inorganic matter, may be readily and completely destroyed merely through the action of acids.

The Miller theory of the etiology of dental caries is in accord with all these facts. This view of the process remains the fundamental working hypothesis. The theory postulates the action of mouth bacteria on carbohydrate food particles stagnated in protected sites at the surfaces of the teeth, the local formation of acids by fermentation, and the consequent focal dissolution of the enamel.

**Experimental Caries in Rats.**—T. Rosebury, M. Karshaw and G. Foley (*Ibid.* 76: 773 (July) 1934) succeeded in producing in the molar teeth of rats what they are satisfied to call true caries. They used a diet consisting of whole, raw, brown rice, plus 8 per cent. of dextrin, and fresh spinach leaves. Rats placed on this diet at 22 days of age developed dental caries in nearly every instance, although not in all of their teeth, after about 5 weeks.

This condition Rosebury and his associates found could be prevented outright merely by grinding the rice particles very finely or by cooking the rice. This confirmed the observation of Hoppert, Webber and Canniff that caries may be produced in rats merely by varying the particle size of cereal in the diet. Even when a diet sufficient in minerals, protein and vitamin D was added to the caries-producing rice diet, fully adequate for growth, maintenance and reproduction, dental caries was not prevented.

The generally accepted view that soft, cooked foods are responsible for dental caries, and that coarse, fibrous diets prevent dental disease by virtue of their assumed cleansing action is at variance with the latest findings in experimental caries in rats.

Variations in the form of the teeth may influence the susceptibility to dental caries.

The so-called lactobacilli may be specifically and exclusively responsible for decalcification of enamel in caries, but their presence is not necessarily a determining factor. They occur at times in caries-free mouths and may be fed to such individuals without doing any harm.

**VINCENT'S INFECTION.**—The *diagnosis* of Vincent's infection of the mouth is a comparatively simple matter, according to I. Hirschfeld (J. Am Dental Assoc. 21·768 (Nov) 1934). It is described generally as a rapidly destructive disease in the wake of which the teeth remain more or less divested of paradontium. The outstanding clinical symptoms are ulceration and sloughing of the marginal gingivæ, especially interproximally. The necrotic layer, yellowish-white or grayish-white, may easily be wiped off its highly inflamed base. The lesion thus exposed is extremely painful and bleeds on the slightest provocation. The ulceration may occur on the mucous membrane of any part of the mouth and throat in the form of yellowish or grayish, white patches with well defined inflammatory margins. The fetid breath, almost always evident, is distinctly characteristic and easily recognizable. These symptoms usually appear suddenly and are often accompanied by a metallic taste, increased salivation and swelling of the submaxillary lymphatic glands, also malaise, rise in temperature and mental depression.

**Etiology.**—Two forms of bacteria are always present in the disease and are said to grow in symbiosis. The causative organisms may be readily identified in smears obtained from active lesions. P. G. Puterbaugh (*Ibid* 21 1925 (Nov) 1934) briefly describes the *Bacillus fusiformis dentium* as spindle-shaped rods with pointed ends. It varies in size from 1·5 to 4 microns in width and from 3 to 10 microns in length. Microscopically it presents a granular appearance, staining irregularly with gentian violet or methylene blue and having from 2 to 6 visible granules distributed throughout its length. The other bacterium omnipresent in Vincent's infection is the thread-like *spirochete of Vincent*. This very delicate organism has from 2 to 5 spirals, is 0·3 microns in diameter, and from 12 to 15 microns in length.

Information is lacking as to how long the organisms are capable of living outside the body. The fact that the disease is frequently transmitted by means of drinking cups, eating utensils, pencils, etc., confirms the belief that they retain their virulence under adverse conditions for a considerable length of time.

Vincent's infection occurs in all parts of the world, but is most prevalent in the temperate zone. Probably because of the reduced resistance of soldiers in the trenches and their subsistence on army rations, all armies engaged in the World War became its victims. Persons of all ages are susceptible, and children frequently contract the disease, especially when living in the same household with adults who have acquired it. It is more common in males than in females, and the widespread occurrence of Vincent's gingivitis in the mouths of cigarette smokers is strongly suggestive that the cigarette may play an important rôle in providing suitable soil for development of fusospirochetal organisms. The high incidence of the disease in direct relation to the increased consumption of

cigarettes is strongly supportive evidence for this belief. It is also quite common in the mouths of women who habitually smoke cigarettes, but it is rare among those who do not smoke. From this observation, and because of the difficulty encountered in its treatment when cigarette smoking is continued, it is the opinion of the writer that the almost universal indulgence in cigarettes is in a great measure accountable for the increase of Vincent's infection in recent years. Malnutrition, avitaminosis, severe metabolic disturbances and diseases of the oral tissues are important predisposing conditions.

**Treatment.**—In selecting therapeutic aids, it should be remembered that in no other infectious disease have so many methods of treatment been suggested. H. Lichtenberg, M. Werner and E. Lueck (J. A. M. A. 100:707 (Mar. 11) 1933) were able to report many cures without treatment. Other writers prescribe no antiseptics at all, depending entirely on **thorough brushing of the teeth** and **mechanical cleansing of the ulcerating surfaces**. Others regard the disease as an avitaminosis and suggest that a quart of **orange juice** with the juice of 3 **lemons** be added to the daily diet. The treatment of Vincent's infection is most uniformly effective when topical applications of **antiseptics** and frequent use of **oxidizing mouth washes** play a prominent rôle.

As a rational therapeutic measure, based upon a knowledge of the anaerobic character of the infective organisms, the antiseptics that destroy bacteria by oxidation seem best adapted to combat the infection. **Hydrogen dioxide** U S P, diluted with equal parts of water, has proved very effective. Freshly prepared **sodium perborate solutions** produce a similar oxidizing effect and possess the additional advantage of being alkaline instead of acid in reaction. These oxidizing agents disintegrate the pseudomembrane overlying ulcerating areas, deodorize putrefying tissue and give a serious setback to anaerobic bacteria.

Topical application of **chromic acid**, in from 5 to 10 per cent solution, is highly recommended

An effective form of treatment consists in first **removing the gray exudate** by gently wiping the infected areas with gauze sponges or by forceful irrigation or spraying with a dilute hydrogen dioxide solution. The ulcers are best dried with warm air and the topical application of 7 per cent aqueous **solution of chromic acid** is made to all surfaces. The home use of **dilute hydrogen dioxide** or a **solution of sodium perborate** every 2 hours for 2 days is prescribed. If the patient's diet is deficient in antiscorbutic vitamins, the juice of 2 **oranges** or **lemons** and at least one **fresh vegetable** daily is to be added.

Treatment should be continued until smears from the gingival crevices fail to disclose the presence of fusiform bacilli and the spirochetes of Vincent, and it is only when negative smears are obtained that the disease may be regarded as cured.

# SURGERY

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# Abdominal Surgery

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**ABDOMINAL SURGERY.—DIAGNOSTIC METHODS.**—The *friction method to determine outline of organs* is discussed by A. Bukovala (Munchen med Wchnschr 81:1026 (July 6) 1934), who recommends this method (1) for abdominal organs—liver, stomach and spleen; (2) for determining to what organs abdominal tumors belong; and (3) for the determination of the lower limits of the heart. The stethoscope is placed with one hand on that region of the skin under which the organ is ordinarily found. At the same time, the forefinger of the other hand makes scraping movements in a definite direction away from the stethoscope. On auscultation, a scraping sound becomes perceptible. As soon as the friction reaches the point corresponding to the projection of the border on the skin, the auscultatory phenomenon disappears or changes in intensity and tone. If the same friction movements are made in various directions from the stethoscope, a number of points are detected the connection of which indicates the outline of the organ.

**LOCAL ANESTHESIA.**—G Bankoff (Lancet 1:287 (Feb) 1934) gives the patient 1 hour before operation an injection of  $\frac{1}{4}$  grain (0.016 Gm) of **morphine** and  $\frac{1}{100}$  grain (0.6 mg.) of **scopolamine**. The operative field is injected with a 1 per cent solution of **procaine hydrochloride**. The injection is made through 2 points equidistant from the line of the incision and radiating over all the field of operation. The needle is then introduced vertically at 2 points on the line of incision until it pierces the internal muscle fascia. At each of these points 20 c c (5 drams) of the fluid is injected. Ten minutes later, the skin and muscle are cut and the peritoneum is exposed, a 2-inch incision is made in the peritoneum through which 200 c c ( $6\frac{2}{3}$  ounces) of a 0.25 or 0.5 per cent solution of **procaine hydrochloride** is poured into the abdominal cavity. Five or 10 minutes later the peritoneum is opened and the necessary operation performed. Excess fluid is taken from the abdominal cavity by means of swabs or a suction pump. For hysterectomy it is advisable to inject a little of the fluid on both sides of the uterus between the 2 folds of the large ligament. This type of anesthesia should be adopted in all patients who cannot stand a general anesthetic, in the opinion of the author.

**OMENTAL GRAFTS.**—In transplantation the thinnest and most vascular area of the omentum available should be used, according to H. F. Graham (Ann Surg 100:96 (Nov) 1934). The graft should extend beyond the raw area to be covered. Fine catgut sutures should be used and placed close together round the circumference of the graft. The raw edge of the great omentum should be turned under and sutured and should not be left in a thick mass to form undesirable adhesions. Success is more likely to follow sharp dissection, a clean field, absolute hemostasis, prompt transfer and accurate suture of the graft to its new location.

**ADHESIONS.—Diagnosis.**—*Leotta's Sign*—F. Rabboni (Polislinico sez chir 41:118 (Mar) 1934) attempted to establish the existence of adhesions in the upper quadrant between the colon and the liver or gall-bladder, according to Leotta, in 100 patients presenting a right abdominal syndrome. Leotta's maneuver consists in placing the hand on the right abdominal quadrant and exerting a downward pressure with the fingers. The traction, because of a downward pull

exerted on the colon below, is painful if the colon is adherent to the gall-bladder or liver. The pain becomes more marked if the patient is asked at the same time to expire forcibly, causing the diaphragm to rise and to displace the liver and gall-bladder upward. To establish the existence of adhesions between the ascending colon and the parietal peritoneum, the maneuver of stretching is applied to the inner part of the right half of the abdomen by making traction with the hand in a transverse direction and from the lateral aspect toward the median line. Thus, if adhesions exist between the ascending colon and the parietal peritoneum, stretching will elicit a sharp pain.

**Prophylaxis.**—In the prevention of abdominal adhesions K. Yardumian and D. H. Cooper (Arch. Surg. 29: 264 (Aug.) 1934) used an **extract of pepsin**, first in hydrochloric acid and then in glycerin, but free from iodine, in their experiments on 44 rabbits on which 104 laparotomies were performed. The abdomen was entered through a midline incision, and the small intestine was rubbed vigorously with a gauze-covered finger for a distance of from 6 to 8 inches in several places. The peritoneum on each side of the incision was forcibly scraped with the sharp end of a scalpel. Before the peritoneum was closed, the pepsin fluid was instilled. Their results show a decreased tendency to the formation of adhesions. The authors assume that the benefit from the digestive action of the pepsin is realized before absorption takes place. The greatest tendency in the reformation of adhesions is observed when trauma is induced in the presence of existing adhesions and their separation, indicating the futility of any effort to prevent reformation of adhesions in cases in which additional trauma is induced.

**ABDOMINAL SURGERY IN CHILDREN.**—J. S. Horsley, Jr. (Virginia M. Monthly 61: 323 (Sept.) 1934) points out that increased and unstable metabolism in children incidental to normal growth renders them more liable to a violent reaction from a slight cause and makes disease sudden in onset and intense in symptoms. The disease may manifest itself in generalized constitutional expressions rather than in focal signs and symptoms. Meyers states that infants require much more water per pound of body weight than adults and that the loss of 10 per cent. of the fluids of the body is grave and 20 per cent. usually fatal. Surgical shock is easily caused and hemorrhage poorly borne, because the proportion of blood to body weight in a child is 1:20 as compared to 1:13 in an adult.

**APPENDICITIS.—Pathology.**—*Fecal Stone*—L. Aschoff (Klin. Wchnschr. 12: 1081 (July 15) 1933) calls attention to the fact that the appendiceal flora in the distal part are most abundant in appendices which show no regular filling and evacuation of feces. The appendiceal flora develop chiefly in the distal part of the appendix because of the physiological curvature of this section of the appendix, by which its evacuation is rendered more difficult. If the appendix has been damaged in its evacuating function by more or less severe attacks of inflammation, the surest sign of the functional disturbance will be a prolonged retention of the feces even when the lumen of the appendix is preserved in its original state and the walls show little macroscopic change. The prolonged retention of the fecal column is not identical with stone. The charac-

teristic stratification of stone formation begins not when the evacuation of feces from the distal part of the appendix becomes difficult, but only after it ceases completely. Stratification begins when a nucleus is formed by sufficient thickening of the fecal mass. Fecal stones contain microorganisms which are typical of the appendiceal flora. Fecal stones do not exert a mechanically destructive effect on the mucous membrane; the most severe inflammation is distal to the stone.

**Diagnosis.**—The *Schilling blood count* is recommended by J. L. Rogatz (J. Pediat. 4.757 (June) 1934), as an aid in the diagnosis of acute appendicitis in children. Of the 30 cases reported, which were operated upon, histologic specimens in 6 were those of normal or nonacutely inflamed appendices, accurately judged by the Schilling count before operation. A count of the immature, non-segmented, polymorphonuclear leukocytes in the differential blood smear is particularly useful in ruling out acute appendicitis and the need for immediate surgery in cases with false symptoms and signs, where the temperature is normal. In the presence of fever there is usually an increase in the stab forms and an element of doubt exists as to whether the appendix or some other part of the body is responsible for the shift. Regardless of the total white cell count or other suspicious signs, a normal percentage of stab cells indicates the absence of acute inflammation in the body and relieves the patient of the need for urgent laparotomy. In practice, if a case with suggestive signs shows a count of more than 10 per cent stab cells, the count should be ignored and the signs followed. There may be acute appendicitis present. If it shows less than 10 per cent stabs, acute appendicitis is hardly possible.

**Treatment.**—On the basis of 150 appendectomies, with a total mortality of 4 per cent., which were performed any time during the attack, *et c.*, even later than 48 hours after the beginning of the disease, A. I. Kogon (Novy khir. arkhiv. 29. 84, 1933) states that he is an enthusiastic defender and adherent of this practice. Operation in the quiescent stage does not assure a favorable post-operative course or favorable healing.

Three cases of *hemorrhage following appendectomy* are reported by J. Rolland (Bull. et mém. Soc. nat. de chir. 60. 449, 1934). In 2 cases the hemorrhages occurred in highly infected foci of gangrenous appendicitis, where the smaller arterioles of the wall were involved. When the scars gave way, the hemorrhage broke loose. In cases of this kind the use of a **Mikulicz tampon** gives good results. It would be useless to attempt ligation of the vessels in such a necrotic area. In the third case the infection extended along the glands by the posterior lymphatics of the ascending colon, forming an abscess which, on coming into contact with the artery, caused it to ulcerate and rupture.

Two cases are reported by A. Ockin and L. Niscevic (Novy khir. arkhiv. 30. 67, 1933) in which **appendectomy** was performed in *hemophiliacs*. **Blood transfusions** should be given before and after the operation. In the *differential diagnosis*, purpura abdominalis should be borne in mind. In one of the cases operated upon, a large hematoma began to form in the ileocecal region and by the fourth day it filled the entire lower right quadrant of the abdomen. Bloody stools were passed. Petechial hemorrhages occurred in the shoulders, chest, neck,

hard palate, conjunctiva bulbi and visible mucous membranes. Primary healing with gradual retrogression of the hematoma and recovery resulted in 4 weeks. The second case was operated upon for recurrent appendicitis during the interval stage. On the fourth day after operation a large swelling appeared in the right half of the abdomen in association with icterus and marked anemia. **Tamponade** of the abdominal cavity was followed by recovery after 50 days.

P. C. Potter (Ann Surg 99:985 (June) 1934) notes that a frequent cause of death in cases of acute appendicitis with diffuse peritonitis was *paralytic ileus*. For the prevention of this complication Potter recommends intramuscular injections of **puitritin (pitressin)**. He states that the initial dose must be given in the absence of distention of the intestines. The first dose is given at the beginning of the operation. The administration of pitressin must be continued at regular intervals throughout the "hypotonic period." Following the final dose, a **colon irrigation** is ordered.

E. S. Jones (*Ibid*, 99:640 (Apr) 1934) has treated 75 cases of *ruptured appendix* complicated by *general peritonitis* by **appendicostomy**. The mortality was 1.4 per cent. When appendicostomy is done, the cecum and ascending colon are drained directly and the pressure is removed from the ileocecal valve. Gas and the other contents of the small bowel move outward through the appendicostomy tube. Peristaltic activity decreases and the patient becomes more comfortable. Beginning 6 hours after the operation, the author instills from 200 to 300 c.c. of a **physiological solution of sodium chloride** into the bowel at intervals of 2 hours until the patient is able to take fluids by mouth. The tube is removed on the sixth or seventh day.

**CHRONIC APPENDICITIS.—Differential Diagnosis.**—*Congenital Pericolic Membrane Syndrome*—W. H. Buermann (Am J Digest Dis and Nutrition 1:196 (May) 1934) discusses a symptom complex simulating chronic appendicitis, for which appendectomy has often been performed with a persistence of pain referable to the right side. Assuming that the usual differential diagnostic factors have been ruled out, (1) there must be a definite anatomic basis in or about the right half of the colon to produce the symptoms that persist after appendectomy for "chronic appendicitis." If anatomic in nature, there must be an abnormal situation present, such as constriction or rotation, in order to produce an altered physiology of the functions of the colon. (2) If the syndromes of "chronic appendicitis" and congenital pericolic membranes and bands overlap, the syndrome arising from the presence of constricting, congenital pericolic membranes remains as a relatively pure clinical syndrome when only the appendix has been removed. (3) If the syndrome arising from the presence of constricting pericolic membranes still is present after appendectomy, correction of the positive factor by sectioning the constricting membranes and bands should relieve the patient. (4) If the symptoms which are considered indicative of congenital pericolic membranes can be classed as a "syndrome," it should be recognizable as such in all age groups. (5) If abnormal attachments of pericolic membranes are congenital in nature, familial or hereditary tendencies can be demonstrated in a reasonable number of patients.

**APPENDIX.—ARGENTAFFINE TUMORS.**—A. Topa, E. C Craciun and D. Caramzulescu (Arch. d mal. de l'app digestif. 24:392 (Apr) 1934) report 2 cases of primary tumor of the appendix. The authors believe that appendicular neoplasms are practically always a complication of chronic inflammation. It is apparently justifiable to admit 3 kinds of epithelial *cancer* of the appendix. The first is the *Kultchitsky-Schmidt-Ciaccio cells*. The second group is the simple *epithelioma* developed from the cells common to the epithelial lining and glandular crypts. Finally, there is the *mucocoele* which may develop from the muciparous cells.

**GALL-BLADDER.—CHOLECYSTOGRAPHY.**—The *results and indications* of cholecystography are commented upon by René Gilbert and M. J. Demole (Presse méd 41:1823 (Nov 18) 1933). The authors state that one inconvenience of the usual method of cholecystography is the long time required after the injection of tetra-iodide before the gall-bladder becomes visible, which generally requires 12 hours. Antonucci has devised a method by which it is rendered visible in from  $\frac{1}{2}$  to 1 hour and reaches its maximum visibility in 2 hours.

The patient is usually prepared by 3 or 4 days of a diet poor in carbohydrates, but this step may be omitted. On the day of the test he is given an intravenous injection of 125 c.c. of a 40 per cent **glucose solution** followed by an injection of **tetra-iodide**. Ten minutes later he is given 10 units of **insulin** subcutaneously. To prevent accidents, both the glucose and the tetra-iodide are injected slowly, each injection taking from 15 to 20 minutes.

The glucose provokes a transitory hyperglycemia which hastens the passage of the tetra-iodide through the liver. The diet poor in carbohydrates decreases the liver glycogen and in this way reinforces the action of the glucose. However, it is not strictly necessary. The insulin furthers the excretion of the iodized bile from the liver into the bile ducts.

The authors have used this method in 50 cases. The results were negative in 47 per cent. This is a higher percentage of negative results than with the Graham method. However, the rapid method gives positive results in some cases in which the Graham method gives negative results, *e g*, in cases of Basedow's disease and diabetes. This is due to the fact that the hyperglycemia hastens the passage of bile into the gall-bladder which is empty when the first x-rays are taken by the slow method.

However, while a positive rapid cholecystogram is conclusive, a negative rapid cholecystogram is not. When the negative results in the cases reviewed were controlled by Sandstrom's fractional oral method, it was found that many of them were positive. With the Antonucci method, some cases that are negative at the end of 2 hours become positive after 5 or 6 hours. Therefore, if it seems probable that cholecystography will be negative, Sandstrom's method is the method of choice, but if a normal gall-bladder picture is expected, the rapid method is preferable.

P. Buisson (Radiol med 21:392 (Apr) 1934), states that, judging from published reports, cholecystography has rendered the problem of the mechanism

of the emptying of the gall-bladder more complicated instead of solving it. Following a discussion of some of the theories which have been advanced to explain the physiology of gall-bladder emptying, he concludes that the emptying results from the contractive activity of the musculature of the gall-bladder. In support of his conclusion he presents evidence obtained in a study of normal or only mildly diseased gall-bladders with the use of egg yolk and x-ray examination. In this study, the important findings of which are shown by x-ray pictures, it was found that filling of the hepatic or common duct took place simultaneously with a decrease in the size of the shadow of the gall-bladder and with filling of the cystic and common ducts. Retrograde filling of this canal suggested not only hermetic closure of the mouth of the common duct where the common duct empties into the duodenum (contraction of the sphincter of Oddi) and filling of the duct to its maximum distention and capacity, but also a *vis-a-tergo* due to contractile activity of the gall-bladder.

**EXPERIMENTAL DATA.**—Following a brief review of the literature, R. Lombardi (Ann. ital. di chir. 12:1509 (Dec. 31) 1933) presents the results of experiments carried out on dogs to determine the relationship between acute bacterial and abacterial *inflammations of the gall-bladder* and changes occurring in the liver. In 2 series of experiments he injected 1 or 2 c.c. of a culture of *Bacillus coli* or *Staphylococcus aureus* and in another series introduced several pieces of sterile glass into the lumen of the organ. After varying periods of time, the animals were sacrificed and the gall-bladder and liver examined.

In all of the experiments a *hyperplastic cholecystitis* resulted, but in the experiments in which only sterile pieces of glass were introduced into the lumen of the organ there were no associated changes in the parenchyma of the liver. In the experiments with bacteria, examination after from 10 to 20 days showed the liver lesions to be few and to consist of a slight infiltration of the interlobular spaces and some connective tissue reaction. After from 30 to 40 days, increased infiltration was found, especially in the spaces of Kiernan, there was a large amount of new connective tissue, especially in the interlobular spaces, and the hepatic cells presented retrogressive changes even to complete disappearance with replacement by connective tissue. In only one instance were small pyogenic foci found in the new connective tissue.

The author states that the hepatic lesions are probably the result of toxic action rather than direct bacterial action. When bacteria occasionally gain access to the liver, they produce foci of suppuration.

From his findings, Lombardi concludes that early intervention is desirable in *acute cholecystitis* in order to prevent marked liver damage, as it is possible that damage to the liver is responsible for the symptoms which persist after late surgical intervention, such as is generally practiced today.

The mechanism of *torsion* of the gall-bladder is explained by C. Mastrosimone (Ann. ital. di chir., 13:385 (Apr. 30) 1934). In experiments carried out on 11 dogs to determine the mechanism of torsion, the gall-bladder was dissected free from the lower surface of the liver so that it hung down free in the abdomen. The neck of the cystic duct was cauterized with a silver nitrate

pencil so that it was partially constricted but not entirely occluded, and from 120 to 200 c.c. of physiological salt solution were injected into the gall-bladder. When the animals were killed after 1 or 2 weeks, torsion of the gall-bladder, varying from about 90° to 2 complete turns, was found in 7 instances. The torsion was greater, the fuller the gall-bladder. The author believes it was due to unequal weakening of the muscle fibers of the wall, the fibers that were less injured initiating the torsion by contracting more strongly than those that were more injured.

The clinical conditions producing such torsion are: (1) chronic distention of the gall-bladder, which elongated and relaxes its mesentery so that in time it acquires abnormal mobility; (2) traction on the organ by adhesions to the stomach and colon; and (3) the presence of many stones causing weakening and elongation of the organ.

**BILIARY FISTULA, INTERNAL.**—Three cases of *cholecystopyloric fistula* and 2 *cholecystoduodenal fistulae* are reported by R. L. Masciottra and M. A. Etcheverry (Rev. med.-quirurg. de pat. feminina 1. 234, 1933). Calculous ileus developed in both cholecystoduodenal fistulae. In one, the diagnosis of cholecystoduodenal fistula was made by x-ray examination before operation. In the other, the fistula persisted for 3 years after operation, although the patient was free from abdominal symptoms.

In 1932, the literature contained the reports of only 42 cases of internal biliary fistula diagnosed by the x-rays. The authors' case is the first to be reported in the Argentinian literature. Of the 4 other cases reported by the authors the preoperative diagnosis was strangulated umbilical hernia in 1, stone in the common duct in 1, and tumor of the pylorus in 2.

In discussing the *x-ray diagnosis*, the authors state that the isolated demonstration of barium in the biliary tract does not always mean an internal biliary fistula, neither is the presence of gas or air in the gall-bladder pathognomonic, as pyopneumocholecystitis must be excluded. In the latter condition, a level surface of the fluid in the gall-bladder and infiltration of the walls with gas are important signs which are absent in cases of biliary fistula.

The authors discuss at length the advantages and disadvantages of **enterostomy** for drainage of the proximal loop in biliary ileus. In the Argentine this operation has not been performed in the majority of cases, but the mortality appears to be lower than that in cases reported from other countries in which enterostomy was done.

**CARCINOMA OF BILE DUCT.**—W. E. Lee and H. P. Totten (Ann Surg 99 930 (June) 1934) report 2 cases of primary carcinoma of the common bile duct causing bile obstruction.

After reviewing the literature, the authors made the following observations.

1. Prevalence of carcinoma of the bile ducts in patients past middle age.
2. Prevalence in the male, 62 per cent.
3. Relative low-grade malignancy of the tumor with considerable amount of fibrous tissue.
4. Prevalence of adenocarcinoma, composed of columnar epithelium.



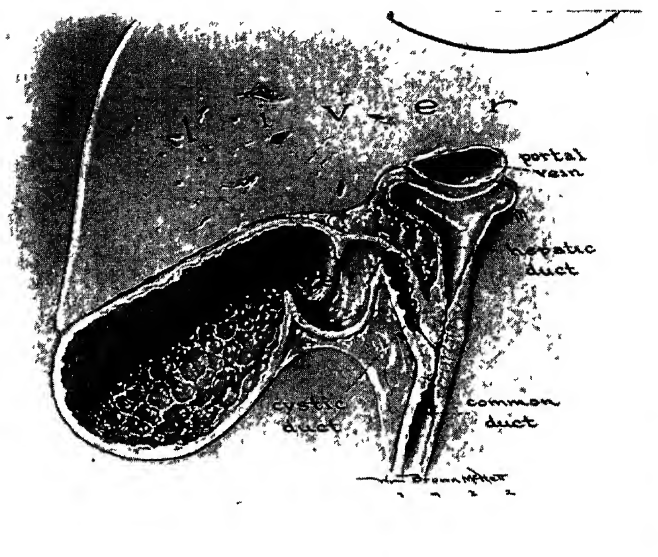


Fig 1—Case I Infiltrating carcinoma of walls of common duct extending from above junction of cystic and common ducts to an equal distance below (Lee and Totten Ann Surg)



Fig 2—Case II Carcinoma involving submucosa near ampulla of Vater (Lee and Totten Ann Surg)

5 Hemorrhage is the most common serious postoperative complication and the most common cause of death

From the practical standpoint, the distinction between benign and malignant tumors of the common duct is more of academic than clinical interest, as on the one hand, the malignant growths are usually small, confined to the duct, slow-growing, and slow to metastasize, while on the other hand, the benign tumors are potentially malignant and are often borderline, that is, they have features both malignant and benign

In both types mechanical interference is responsible for the disturbed chemical and physiological processes, expressing themselves clinically in hemorrhage and cholemia.

The conclusions to be drawn are that (1) the symptoms of primary cancer of the common bile duct are not pathognomonic. They may be suggestive, but in final analysis they are simply the symptoms of mechanical biliary obstruction.

(2) It is important to consider the possibility of a primary malignant growth in all cases of persisting obstructive jaundice in patients past middle life. The presence of one or more gall-stones in the common duct should not lead the surgeon to neglect a complete exploration of the ducts.

(3) **Early operation** is urged with thorough and painstaking exploration of the common duct for possible malignancy in all suspicious cases.

(4) The high mortality which attends operations for biliary obstruction due to primary cancer is due almost entirely to complications resulting from mechanical obstruction of the biliary tract.

(5) Postoperative hemorrhage following the relief of mechanical biliary obstruction is responsible for the high percentage of deaths.

(6) Diabetes complicating biliary obstruction is particularly dangerous, due to grave metabolic disturbance.

(7) Early diagnosis and early operation will tend to lower the mortality rate, not only by minimizing the chance of extension of the primary growth, but by decreasing the incidence of complications due to obstructive jaundice, *viz.*, hemorrhage, hepatic insufficiency and cholemia.

**CHOLECYSTITIS, ACUTE.**—A. S. W. Touroff (Ann Surg. 99. 900 (June) 1934) states that acute inflammatory changes may be present in the gall-bladder of a patient who presents only minimal or no clinical manifestations at the time of operation. The pathological changes found in 75 such cases ranged from simple acute to hemorrhagic, phlegmonous suppurative, and gangrenous inflammation, empyema, perforation, and pericholecystic abscess. In general, the patients with minimal manifestations showed a considerable higher incidence of advanced and progressive lesions than the patients without manifestations at the time of operation. Eighty per cent of the lesions in the series were considered conservatively to be subsiding or capable of subsiding. The remaining 20 per cent were considered progressive. It is impossible to determine the exact nature and extent of the inflammatory lesion before operation.

**Treatment.**—In cases of acute cholecystitis in which subsidence once begun does not proceed uninterruptedly, fairly promptly, and completely, Touroff (*Ibid*) considers that **early operation** is indicated. In cases of acute cholecystitis with subsided clinical manifestations, operation, early rather than late in the interval, is indicated because of the danger of the existence of a silent acute lesion.

Important factors in the **surgical treatment** of cholecystitis are discussed by H. F. Graham and H. S. Waters (*Ibid* 99. 893 (June) 1934) who report 60 gall-bladder operations with 4 deaths. Pulmonary and cardiac complications are those most to be feared. For reduction of the incidence of pulmonary complications the authors offer the following rules.

1. Eliminate the binder
2. Avoid large doses of the barbiturates
3. Use **morphine** in moderate doses for the relief of *pain*.

4. Place the patient in the **sitting position** to aid the accessory muscles of respiration and take the weight of a heavy abdomen off the diaphragm.

5. Give inhalations of **carbogen** for 5 minutes every 2 hours for at least 24 hours.

6. Teach the patient to **breathe deeply** every 15 or 20 minutes.

7. Prevent chilling.

The administration of carbohydrates both by **diet** and by the intravenous injection of **glucose** immediately before the operation is indicated because of the usually associated hepatitis.

The authors emphasize the importance of **early operation** in cases of acute cholecystitis.

**GALL-BLADDER STASIS.** — *Pathogenesis.* — The clinical concept of congestive gall-bladder should probably be retained, although it is necessary to exclude from the large number of supposed cases of this condition a not small number in which the diagnosis is erroneous, *i e*, cases of gastric and duodenal ulcer, chronic duodenal obstruction, appendicitis, and kidney lesions. C Brzozovskij (Novy khir arkhiv 28:164, 1933) points out that in the production of colic in the congestive gall-bladder, mechanical disturbances to the flow of bile, infection, and dyskinesia of a neuro-functional nature are the most important factors. After subtraction of the cases due to these factors, there remains a smaller group which represents a transitional form between dyskinesia and cholelithiasis, to which the term "*congestive gall-bladder*" is most applicable.

The author's material confirms the opinion of others that in most cases congestive gall-bladder is the initial stage of a *stoneless cholecystitis*, and that a sharp line of demarcation cannot be drawn between the two conditions. However, it cannot be concluded from this that all cases of stoneless cholecystitis have their origin in congestive gall-bladder. In some cases the congestive gall-bladder and stoneless and calculous cholecystitis are successive stages of one and the same inflammatory process. There are also numerous cases in which the disease develops in the following sequence: dyskinesia, congestive gall-bladder, stoneless and calculous cholecystitis. However, every case of stoneless calculous cholecystitis must not be considered as a stage of one and the same infectious process. Stones may be formed without infection, as the result of a disturbed chemism (cholesterin diathesis, Bourhard, Aschoff) and the calculous form may change into the stoneless form after passage of the stones into the bowel.

In outlining the surgical treatment of gall-bladder stasis, O Lambret (Presse méd 41:1097 (July 12) 1933) states that diseases peculiar to the infrahepatic region may be classified into 2 groups: (1) ulcer, cancer, cholelithiasis, and the inflammatory results of cholelithiasis; and (2) certain more or less functional disturbances which are differently interpreted by various authorities. It is with the second group, particularly gall-bladder stasis, that this article deals.

In spite of the important studies of Lyon and Chiray, there has been no unanimity of opinion regarding the diagnosis, the nature, or the treatment of gall-bladder stasis. In Lambret's opinion, the essential feature of gall-bladder stasis is *visceroptosis*. This may or may not be complicated by perivesicular adhesions.

When perivesicular adhesions are present, the stasis is atonic, and when they are absent, it is mechanical and atonic.

In atonic stasis, the gall-bladder is elongated and mobile and extends beyond the edge of the liver. It can be emptied readily by compression, but remains flaccid. In addition to the "cholecystatony" described by Chiray, there is ptosis. In 6 per cent of the cases, calculi are found. Cholecystitis is exceptional. Beside the gall-bladder findings, there is the general picture of visceroptosis, and the atony extends to the stomach and duodenum.

When the stasis is due to a mechanical cause, such as *perivesicular adhesions*, ptosis may be absent. However, it is present in 8 out of 10 cases. Because of the associated disorders in the infrahepatic region, the rôle of the gall-bladder in the production of symptoms is difficult to determine exactly. Pain over the gall-bladder, asthenia, headaches, vomiting, and icterus are symptoms of some significance. Drainage by the Lyon method occasionally produces an abundant amount of bile and is followed by relief for a time. The most valuable *diagnostic method* is cholecystography. This shows a persistent gall-bladder shadow and discloses the shape and location of the gall-bladder.

The functional effects of stasis are easily understood. The bile becomes abnormally concentrated and viscid, making evacuation of the gall-bladder difficult or impossible. The result is discomfort or pain in the right hypochondrium. The condition becomes more complicated when there are adhesions between the gall-bladder and duodenum.

**Treatment.**—While treatment by the method of Lyon often gives good results lasting for a period of 2 or 3 months, some patients are unable to tolerate it and few are benefited by it for a considerable length of time, according to Lambret (*loc cit*).

**Surgical methods** of treatment include cholecystectomy, external drainage, and internal drainage.

Cholecystectomy does not give relief and often aggravates the condition.

**External drainage** is of value when cholecystitis or pancreatitis is present. In cases of stasis alone, the patient is relieved only as long as the fistula persists.

**Internal drainage** by anastomosis of the gall-bladder to the stomach or duodenum is not a physiological operation. While the results are sometimes excellent, they are also sometimes very poor.

As *ptosis*, particularly of the stomach, is the essential feature in these cases, the author believes that operation should be directed primarily to the ptosis and procedures on the gall-bladder should be accessory. At operation, the gall-bladder may be found normal, atonic, or obstructed. When it is normal, the operation should be limited to **plication and suspension of the stomach**. When ptosis and atony of the gall-bladder are found, plication and suspension of this organ should be added. The fundus should be reduced by invagination beneath a purse-string suture.

If the ptosis is due to anomalies of position, with kinks of the cystic duct within the lesser omentum, the duct should be isolated in order to destroy adhesions and in order that it may be straightened. The resulting defect in the peritoneum may be repaired with a peritoneal or prepared graft of amniotic

membrane. Adhesions to the duodenum are particularly serious. They must be destroyed and their recurrence prevented. The raw surface of the gall-bladder should be covered with a prepared graft and that of the duodenum is invaginated by a transverse suture. This suture displaces the duodenum to the left and out of contact with the gall-bladder.

In some instances duodenal stasis necessitates **duodenojejunostomy** in addition.

The operations described are well tolerated. The author obtained satisfactory results from them in a series of 120 cases. In the oldest cases, the results have been maintained 6 years.

**GALL-STONES.—*Diagnosis.***—The study of crystalline elements in the stomach lavage of patients with cholelithiasis has been undertaken by H. A. Rafsky (J. Lab. and Clin. Med. 19: 959 (June) 1934). He states that cholesterol and carbonate crystals and calcium bilirubinate pigment were found, separately and collectively, in appreciable amounts in the stomach lavage of a group of patients suffering from calculous cholecystitis. The presence of these crystalline elements in the gastric lavage was due to regurgitation of the bile and duodenal contents into the stomach. In about one-half of the patients the gastric lavage water was bile-tinged and in the remaining patients it was colorless.

Although biliary crystals were present in the stomach lavage in appreciable amounts, they were not, as a rule, as numerous as the crystals seen in pre-operative specimens of bile of patients with cholelithiasis. When, however, the gastric lavage was performed within 6 hours after the onset of an attack of biliary colic, showers of crystals and an abundant amount of calcium bilirubinate pigment were found.

Carbonate crystals in the stomach lavage were dissolved by hydrochloric acid, which aided in differentiating these crystals from the atypical types of cholesterol crystals. At times, starch granules in the lavage water had to be distinguished from biliary crystals. This was readily done by the addition of iodine.

Microscopic examination of the stomach lavage of the patients in the control group did not reveal any cholesterol or carbonate crystals; yet, a slight amount of calcium bilirubinate pigment was found in 4 of the patients. In a previous paper H. A. Rafsky (Am. J. M. Sc. 185: 851 (June) 1933) emphasized that a few cholesterol crystals or a small amount of calcium bilirubinate pigment present in preoperative specimens of bile had no pathologic significance. The presence of a slight amount of calcium bilirubinate pigment in the stomach lavage, likewise, cannot be regarded as abnormal.

The presence of biliary crystals in the stomach lavage of patients with cholelithiasis is of some significance. However, an exact diagnostic appraisal of this finding cannot as yet be given, as the subject is still under investigation.

***Pathogenesis.***—The experiments of H. B. Weiser and G. R. Gray (Arch. Path. 17: 1 (Jan.) 1934) on the mechanism by which precipitated cholesterol may be collected into a unified coherent mass show that: (1) Precipitation of cholesterol in the gall-bladder is in itself altogether inadequate to account for the formation of pure cholesterol concretions. (2) Experimental observations have

been made which furnish the basis of a mechanism to account for the formation of such concretions during biliary stasis resulting from anatomic or physiologic abnormalities. (3) By the proposed mechanism, gall-stones have been synthesized which simulate the natural concretions in both macroscopic and microscopic appearance and in properties. (4) Particular attention has been called to the importance of fat in the formation of pure cholesterol concretions, both as a collecting agent for the minute particles of precipitated cholesterol and as a solvent that is responsible for the growth of interlacing crystals into a concrement.

The pathogenesis of gall-stones and function of the gall-bladder are set forth in the experimental investigation of J. H. Cascao de Anciaes (*Arq. de pat* 6 5 (Apr.) 1934). In experiments on 67 dogs he followed up the formation of precipitates and concrements in the gall-bladder from the first traces of precipitation to the definite formation of stones. In other experiments he studied the function of the gall-bladder mucous membrane, especially its concentrating capacity and secretory function. When the cystic duct was ligated an amorphous bilirubin precipitate was formed in 45 minutes. Later, the precipitates and concrements disappeared as the result of transformation of the bilirubin into biliverdin brought about by the mucus and oxydases of the gall-bladder.

When inflammation of the gall-bladder mucous membrane was produced by mechanical irritation and infection, the inflammation caused cholesterol precipitates that were not seen in simple stagnation. On faradic stimulation of the vagus with ligation of the cystic duct, macroscopic concrements were formed in 2 hours. Stimulation of the vagus also caused the precipitation of cholesterol and lipid infiltration of the mucous membrane.

In another series of experiments the author studied variations in the concentration of bilirubin and cholesterol following variations in the size of the gall-bladder caused by stimulation of the vagus. He found that the increase in concentration exceeded the reduction in the size of the gall-bladder. From this he concluded that bilirubin and cholesterol are produced by the gall-bladder wall, either by excretion or by a reexcretion similar to that which takes place in the intestine. He found also that the gall-bladder epithelium excreted dyes and iodine given parenterally, an observation which supported his theory that the epithelium has excretory functions.

From the embryological development of the gall-bladder he concluded that its mucous membrane secretes ferments. After ligation of the cystic duct in experiments carried out to prove this theory, he found protease, amylase, and lipase, and noted that the amount of lipase increased under the stimulating action of pilocarpine and histamine, while the amylolytic and proteolytic ferments showed no appreciable change. He believes that the gall-bladder lipase is secreted by the glands of the gall-bladder in a manner similar to that in which intestinal lipase is secreted, and that its function is to split cholesterol before it is absorbed by the mucous membrane. He found that histamine caused pancreatic hypersecretion independently of gastric hypersecretion. In a study of the diffusion of bile in dialysis tubes, he found that the pigments acted like diffusible salts. He believes that when the mucous membrane is inflamed it acts as a dialysis membrane,

preventing the absorption of cholesterol and permitting dialysis of pigments, thus producing the white bile of gall-bladder hydrops and pure cholesterol stones.

**Treatment.**—For many years, B. Schiassi (J. de chir 43 8 (Jan ) 1934) has been reluctant to remove the gall-bladder and since 1900 he has been an active opponent of **cholecystectomy** as a routine measure. Whenever possible, he has limited operation for cholelithiasis to evacuation of the gall-bladder followed by complete closure, believing that the gall-bladder possesses important function and, therefore, should be conserved.

When the sphincter of Oddi opposes the flow of bile into the duodenum, the gall-bladder acts passively as a reservoir. While the bile remains in the gall-bladder, it is concentrated 5 times by removal of part of its water content. By active contraction (the claims of Winklestine notwithstanding) the gall-bladder empties its contents into the duodenum at the moment when the chyme is most abundant.

Following cholecystectomy, the sphincter of Oddi loses its tonicity and the flow of bile into the duodenum becomes continuous or the tonus of the sphincter is retained and the common duct and the hepatic ducts with their first branches become dilated and assume the function of the gall-bladder.

The *pathological changes following cholecystectomy* include progressive destruction of the epithelium and fibrosis of the walls of the larger bile ducts, conditions favoring infection of the biliary tract; an increase in intestinal putrefaction and in the virulence of the intestinal flora; reduction of pancreatic secretion by at least two-thirds (Iverson), and, interference with the digestion of fat. These are the intrinsic effects of the operation. Possible extrinsic effects include pancreatitis, pericholedochal adhesions, periduodenitis and pericolicitis with adhesions and stenosis, and biliary fistula. Because of the frequency of these complications, Rosenthal said, "Never promise a patient about to undergo cholecystectomy that he will not suffer after the operation." The mortality from peritonitis, hemorrhage, shock, and hepatic degeneration after the operation is not inconsiderable. The hepatic changes are especially important.

Schiassi performs **cholecystectomy** only when the walls of the gall-bladder are altered to such a degree that the function of the organ as a contractile reservoir is seriously limited. He states that in cases in which the gall-bladder wall is only moderately thickened, the mucosa is only slightly ulcerated, and the serosa is smooth and pale, **cholecystostomy** is sufficient. When the serosa is smooth, the other tunics are little thickened, and the mucosa is free from ulcerations, **cholecystendysis** is the operation of choice. This consists in liberation of the gall-bladder and evacuation of the calculi, followed by complete closure. It was first performed by Loreta, of Bologna, in 1875. The author and his colleagues have obtained satisfactory results from cholecystendysis in 314 cases.

The incidence and management of stones in the common and hepatic ducts is discussed by F. H. Lahey (Ann Surg. 98:644 (Oct ) 1933). Up to the year 1926, Lahey had operated upon 619 patients for biliary tract disease (infection and stone). In this group he opened the common or hepatic duct to remove or explore for stones in 15 per cent. of the cases. As a result of these investiga-

tions of the ducts, stones were discovered and removed in 8 per cent. of the cases. The mortality in this group was 5.6 per cent.

In looking over the follow-up figures at this time, Lahey became impressed with the fact that a good many patients had persisting symptoms of cholelithiasis following cholecystectomy, due to stones being left in the ducts. He, therefore, began to investigate hepatic and common ducts more generally and upon less and less positive evidence of the probable presence of stones.

A table is submitted showing the gradual increase in the number of cases in which the ducts were opened, together with the percentage of cases in which stones were demonstrated and removed, and the mortality rate for each period.

Years	No of Cases of Duct Stones	Percentage of Ducts Opened	No. of Stones Found	Per Cent	Total Cases	Gall-stone Mortality
1910-1926	96	15 <sup>5</sup> 4	52	8 <sup>4</sup>	619	5 <sup>8</sup>
1927-1928	91	32 <sup>7</sup>	38	13 <sup>7</sup>	278	1 45
1929	49	35 <sup>8</sup>	22	16 <sup>1</sup>	137	3 <sup>8</sup>
1930	61	42 <sup>5</sup>	30	21	138	2 <sup>1</sup>
1931	45	38	22	19	116	3 <sup>4</sup>
1932	52	46	24	21 <sup>2</sup>	113	1 <sup>7</sup>

Lahey assumed from the above figures that a common- or hepatic-duct stone was left in at least 1 of any 10 cases of gall-stones operated on prior to 1926. This, in his opinion, is a very undesirable situation, since a stone, particularly at the lower end of the common-duct at the ampulla, is not only capable of bringing about a serious situation, but in many of the cases it is the stone which is producing the symptoms for which the operation is done.

Lahey feels that it must be concluded from these figures that the absence of jaundice is by no means a trustworthy argument against exploration of the ducts for possible stone. When in over a third of the cases in which duct stones were discovered and removed, the feature which has been considered so typical of the disease (jaundice) was absent, it becomes evident that frequently ducts must be explored upon suspicion, even when no stones can be palpated in the ducts.

In over a third of the cases in which stones were demonstrated and removed but no jaundice was present, Lahey has been unable to palpate stones at the time of operation, and the ducts have been opened and explored without any positive evidence of the presence of the stones. Lahey has now removed stones so often from the lower end of the common duct at the ampulla in the absence of jaundice, and without being able to say definitely that they were there either from the history or by palpation of the ducts, that he is no longer surprised when a stone forcep or sucker, passed down the common duct in a case in which stone would ordinarily not be suspected, is withdrawn with a stone in it.

Lahey believes that when **cholecystectomy** is being done for gall-stones, the *common and hepatic ducts should be explored* (1) whenever on palpation, a stone can be felt, or is suspected, in the duct, (2) when the common duct is dilated, and when the common duct is definitely thickened. He believes that the longer infection and stones have been present in the gall-bladder, the more fre-



quently will stones be found in the common and hepatic ducts, for which reason the ducts should be opened and searched for stones whenever the gall-bladder is found thickened or contracted. Thickening of the head of the pancreas, from whatever the cause, makes palpation of the lower end of the duct for stones

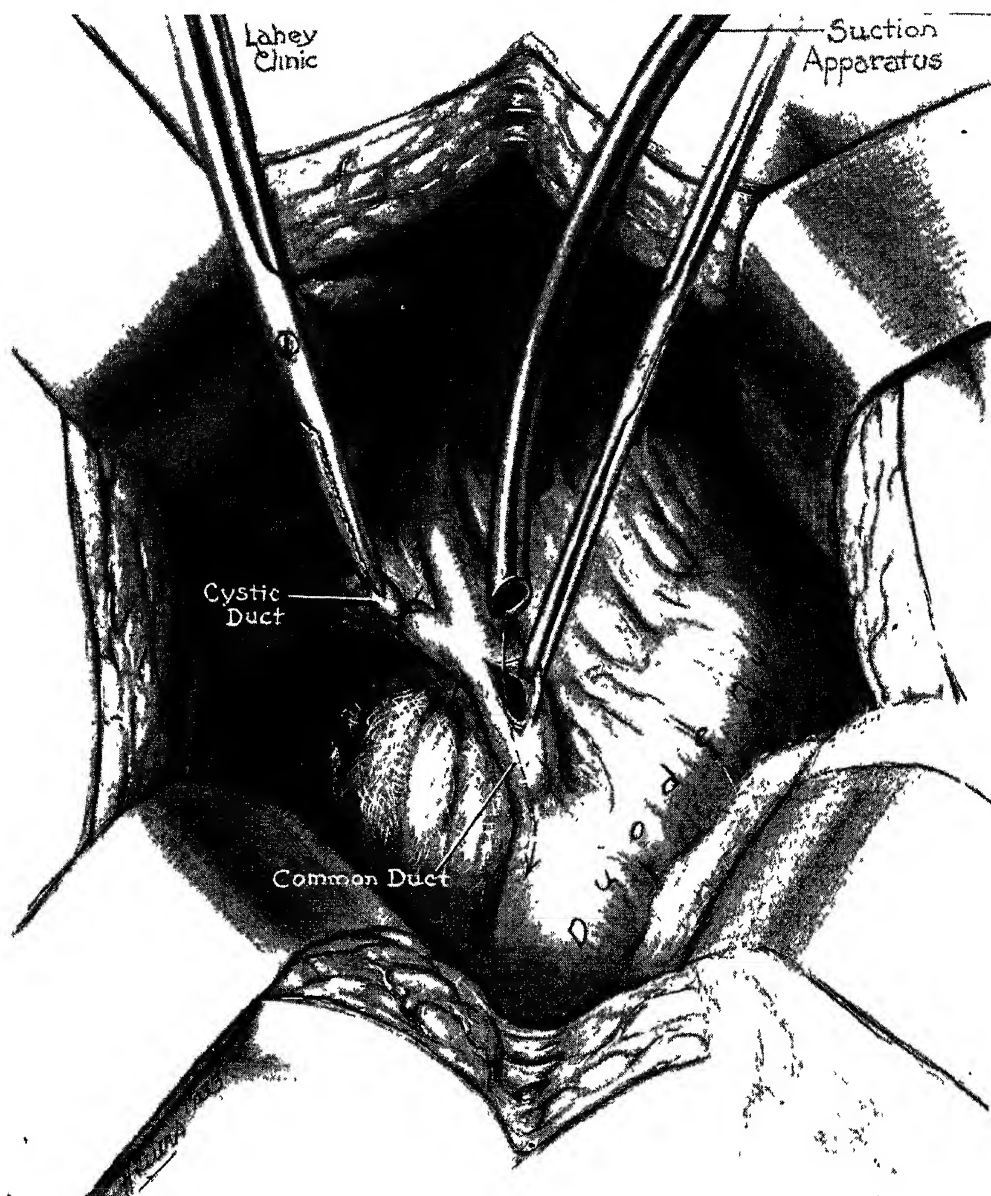


Fig 3—Showing large open ended metal suction tube to be passed down the common duct to the ampulla where stones are so commonly overlooked. Note packing which walls off the foramen of Winslow and also catches any infected material coming from common duct when it is opened. With proper suction technic there should be no contamination of subhepatic spaces with this material, one of the causes of subdiaphragmatic abscess (F. H. Lahey Ann Surg)

uncertain and unreliable. In such cases, also, he believes the common duct should be opened and its lower end explored. (3) Obviously, he believes that the duct should be opened and explored in all patients with gall-stones who are or have been jaundiced.

The safest and most satisfactory way to remove stones from the common duct at the ampulla of Vater, where they are most commonly overlooked, is by passing instruments through the incised common duct down to the ampulla and withdrawing the stones through the duct. When this is possible—and it usually is—it is a much safer procedure than transduodenal choledochotomy or rotation of the duodenum and incision of the duct on the posterior wall of the duodenum.

Large stones lodged at the lower end of the duct usually cause marked dilatation of the ducts, and so make demonstration of the stones and their removal through the ducts relatively easy.

It is the small stones lodged at the lower end of the ducts which are so often overlooked and it is in these cases that the employment of suction has proven so valuable.

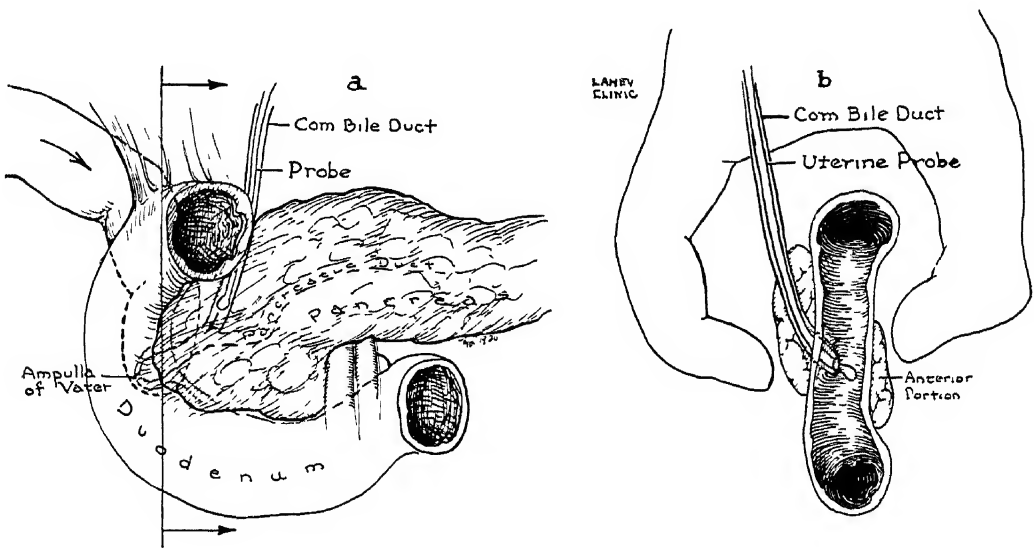


Fig. 4—Plan of passing a uterine probe (a) down the common duct into the duodenum (b), and demonstration of stones at ampulla by palpating them (b) on obturator (F. H. Lahey Ann Surg.)

For the past few years, Lahey has passed a large open-ended metal suction tube, as shown in Fig. 3, down to the ampulla and in many of the cases successfully extricated small stones with it. This scheme has proven valuable in the removal of small stones which might or might not pass, but, when possible, are better removed.

Another method of determining the possible presence of small stones at the lower end of the duct which has proven helpful is by passing a uterine probe down to and, if possible, through the ampulla. Palpation upon the probe, as shown in Fig. 4, will then sometimes permit of the small stone being felt as it is palpated against the obturator within the duct.

One of the most difficult decisions to make in patients suspected of having common-duct stones is to advise operation on the unjaundiced patient who has had cholecystectomy for gall-stones, but who still has pain which is suspected of being gall-stone colic. In such cases, the surgeon constantly has in mind how chagrined he will feel to have put such a patient through another operative pro-

cedure if exploration of the ducts at the second operation proves negative for stone. It is in these patients that duodenal drainage and the study of the sediment of the material so obtained has proven of such great value. Allen Wilkinson, who has interested himself in this situation, has done **duodenal drainage** in 32 patients in whom such a decision has had to be made. On the basis of the demonstration of crystals and bilirubin pigment in all of these cases, he has advised operation. Of the 32 cases, stones were removed from the ducts in 30 and failed of demonstration in 2 instances. The study of the sediment of the material removed by duodenal drainage (Fig 5) has also been of great value in

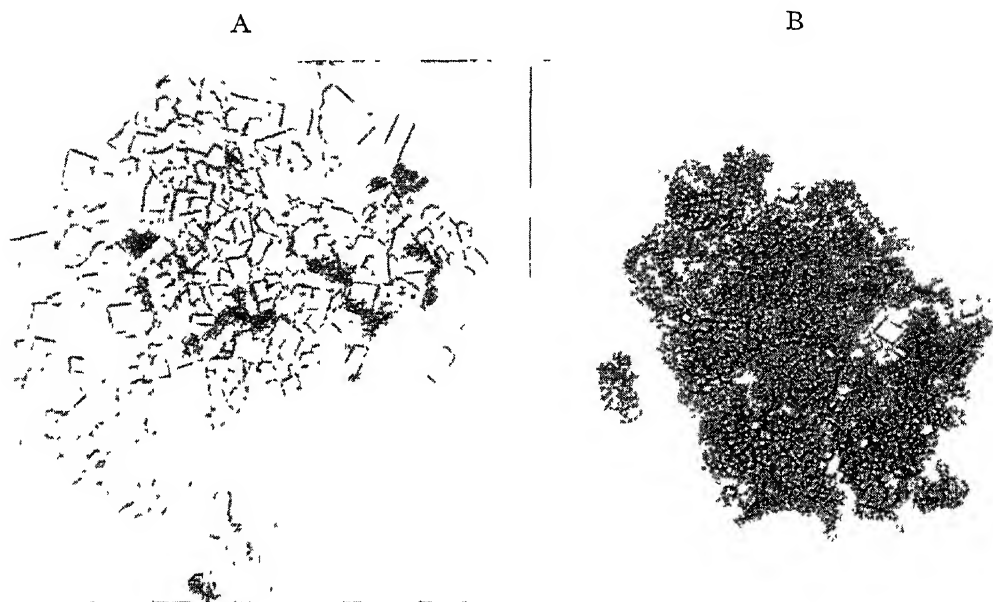


Fig 5—*A*, Duodenal drainage sediment in a patient suspected of and proven at operation to have common-duct calcium stones. This sediment consists of calcium bilirubin pigment and cholesterol crystals. *B*, Cholesterol crystals and traces of pigment in a patient suspected of and proven at operation to have a cholesterol common-duct stone (F H Lahey Ann Surg)

making decisions against surgery in borderline jaundiced cases without convincing evidences of stones in the ducts

From a study of 42 cases in which the common duct was **drained through the stump** of the cystic duct, M M Zimninger and H G McCandless (Surg Gynec. Obst 59:781 (Nov) 1934) conclude that this should be the method of choice when drainage of the duct is necessary. It allows complete and accurate suture of the exploratory incision, which predisposes to early, firm healing of the incision with minimal scarring. It provides a long, narrow channel for the drainage tube, which ordinarily remains watertight until it is time to remove the tube. Removal of the tube causes little damage or disturbance to the common duct, and drainage of the bile from the wound after the removal of the tube is of short duration. The method, therefore, reduces the total loss of bile and shortens materially the duration of the convalescence.

**SURGERY OF GALL-BLADDER.**—The *electrosurgical obliteration* of the gall-bladder is described by M. Thorek (J A M. A 103:169 (July 21) 1934). The procedure may be carried out under **general** or **spinal anesthesia**.

Following ample exposure with mobilization of the falciform ligament, the gall-bladder contents are aspirated and the biliary passages explored. Double ligation and division of the cystic duct and artery are then done and the redundant part of the gall-bladder wall is removed by means of a special diathermy scissors with simultaneous coagulation of the branches of the cystic artery coursing in the gall-bladder wall. Only the portion of the gall-bladder wall which is attached to the bed of the gall-bladder is permitted to remain. This is slowly coagulated to the desired depth. The edges of the coagulated segment of gall-bladder are then approximated with catgut sutures and the falciform ligament is attached to the coagulated area by sutures previously left long. No drains are used.

This method was used in a series of 75 consecutive unselected cases without a fatality. Its value lies in (1) the possibility of obliterating and covering the gall-bladder bed which contains capillaries and often larger bile ducts that, if not obliterated, often cause bile leakage; and (2) the omission of drainage, which favors bile seepage.

**Results of Biliary Tract Operations.**—It has seemed to T. R. Brown (Am J Digest Dis and Nutrition 1:221 (June) 1934) that it may be of interest for a medical clinician carefully to analyze the results of treatment in biliary tract disease, be that treatment medical, surgical or a combination of both; most of the previous analyses have been made by surgeons. It would seem helpful to determine from the point of view of the clinician, who sees these patients over a long period of time, the number that has really been cured or materially helped and the number in whom discomfort, pain, indigestion or other symptoms remain, and then to compare the figures with those of the surgeons.

No one can gainsay that as regards the *diagnosis* of gall-bladder disease, tremendous advances have been made in the past few years: the x-ray studies by the Graham method, analyses of the duodenal contents in certain cases, ever-increasing knowledge of the clinical pictures of gall-bladder and biliary tract disease, a knowledge which has been brought about, primarily, by ever closer co-operative efforts between surgeon and clinician in the study of these affections.

Notwithstanding all these advances, however, there still is a considerable diversity of opinion as to the correct appreciation of symptoms and signs, and of management in many of these patients: chronically diseased gall-bladder with gastric dyspepsia, gall-bladder with symptoms referred elsewhere, those with attacks of biliary colic at long intervals, etc., although, of course, it is quite obvious that in certain conditions (as, for example, repeated and severe attacks of gall-bladder colic, empyema of the gall-bladder, fulminating cholecystitis), one, and only one, method of attack is justified, and that is the surgical.

It is a consideration of these principles as to etiology, diagnosis and therapy based on the newer knowledge, and with a rather extensive personal experience in this field, which led the writer to prepare this paper. How shall these questions be answered?

1. Has the patient gall-bladder trouble, and if so, what is its nature and severity?

2. With gall-bladder disease certain or probable, what is the proper treatment?

In the clinic at the Johns Hopkins Hospital something more than one-fourth of the operated patients—subjects chosen with great care as fit for surgery by a conference of surgeons and clinicians—return complaining of the same symptoms or different symptoms, but complaining! J. T. Howard (*Ibid*, p 270) reports in complete detail the results of the analyses of 84 cases in private practice on whom Brown had advised surgery and where it was possible to find out exactly what the ultimate results of the operation were. On 63 of these patients, cholecystectomy had been performed; on 13, cholecystostomy, on 1, cholecystogastrotomy; on 1, choledochotomy; and on the remainder, the separation of adhesions. Among 4 cases, 1 had a cholecystectomy done following an earlier cholecystostomy.

The *surgical mortality* was 4.7 per cent, a little higher than the 3.6 per cent. of Eusterman's series in 804 cases. Of the series, 59 per cent had complete cure, relative cure, or relief from the disagreeable symptoms, but this leaves the rather striking figure of 41 per cent. in which operative treatment was unsuccessful—a figure sufficiently high to suggest great care in reaching a decision in each individual as to whether surgical or nonsurgical treatment is the better procedure.

The author cannot feel that surgery should be indiscriminately advised for all cases of gall-bladder pathology. It has a definite mortality; it has a considerable proportion of failures; it has many postoperative possibilities which may make the second state of the patient the same as, or even worse than, the first.

Brown believes that in those cases where the clinical picture is a severe one—a very clear cut one, with very marked local or general symptoms—surgery is the only safe reed upon which to lean. In the milder, less definite, and more chronic type of case, it seems better, in view of present knowledge, first to try the simpler and perhaps safer medical measures. Many cases so managed remain symptomatically cured if they are willing to follow a certain regimen, and this, not an onerous one, some, and not a negligible portion, may later have to have recourse to surgery, either because they tire of such a regimen or because they do not get sufficient relief from it to warrant a continuation.

*Conclusions*—The author is sure that it is wrong to consider the gall-bladder as a separate entity and not as a part of the entire biliary tree, although in a considerable proportion of cases, the major portion of the pathology is concentrated there and it is in this group of cases where surgical attack upon the gall-bladder is likely to be most successful. The author is convinced that, in analyzing the symptoms, it must be determined how many are referable to the gall-bladder itself, how many to liver, ducts and biliary tract, for on the results of such analysis the decision as to medical or surgical treatment must rest, and, if the latter is decided upon, what is the best operative procedure?

Brown is quite convinced that **cholecystectomy** is the operation of choice in the vast majority of cases in which surgery is indicated, and that in a good many of these cases complete relief may be obtained by the removal of the gall-bladder. The author is equally convinced that where there is evidence of extensive liver and biliary tract infection as well, it is far wiser, if surgery is to be done, to

employ **cholecystostomy**, possibly followed later by **cholecystectomy** or **cholecystogastrostomy**.

The author has also touched upon the physiological basis for medical and dietetic treatment and its simplicity and its success in a fair number of chronic cases if carried out conscientiously, but he has tried not to overemphasize its value, because surgery must be utilized in most of the severe and many of the milder cases. Finally (for, after all, what is the value of treatment if diagnosis is not correct?), he has tried to preach the doctrine of thoroughness in reaching a final conclusion as to the underlying pathology: he has insisted upon the absolute necessity of a careful history of the case, as well as the utilization of all the laboratory methods at the clinician's command. He has pointed out the difficulties in diagnosis in this field because of the striking tendency of the gall-bladder to mirror symptoms due to disease elsewhere and, in turn, to be the cause of referred symptoms.

According to E. A. Graham and W. A. Mackey (J. A. M. A 103:1497 (Nov. 17) 1934), several writers have called attention to the frequency of unsatisfactory results after **cholecystectomy** on patients whose gall-bladders showed a minimal amount of change from the normal condition (Whipple, Muller, Judd, Stanton and others). The observation, therefore, that surgical results in the stoneless gall-bladder, on the whole, are not so satisfactory, as in those cases in which gall-stones are present, is not by any means new.

In most other conditions the idea has gained ground that a disease should be attacked early in order to obtain the most satisfactory therapeutic results. Alvarez has even suggested that the same principle holds true in cases of cholecystitis. There is some reason to believe, however, that this principle does not hold for diseases of the biliary tract. Indeed, if one were to be guided only by a table of comparative results obtained by cholecystectomy in cases of minimal pathologic change as compared with those which showed marked and definite changes, the conclusion might be reached that the statistical results proved the point that cholecystectomy should not be undertaken in the early cases of cholecystitis before well-marked changes have occurred.

Graham reviews certain features based on a study of 161 patients who were operated on at the Barnes Hospital but who had no stones, except in the cases of 17 who had a combination of cholesterosis with stone. The latter cases were added because by some the conditions of cholesterosis and of cholesterol stones are considered to be expressions of a disturbed metabolism, rather than of a definite disease of the gall-bladder. All the patients who comprised this study had had a cholecystectomy more than a year before they were reexamined to determine the results.

The 161 patients whose condition was ascertained more than a year after operation were classified, according to pathologic lesions, as follows: minimal lesions 57; cholesterosis, without stone, 31; chronic catarrhal cholecystitis, 51; chronic fibrous cholecystitis, 5; cholesterosis with stone, 17.

The term minimal lesion was assigned to those cases in which the gall-bladder wall was not greatly thickened, the organ contained concentrated bile, and on microscopic examination there were a few lymphocytes in the wall. A diagnosis

of cholesterosis was made when the mucosa of the gall-bladder contained the yellowish plaques that are characteristic of lipid deposits. *Chronic catarrhal cholecystitis* was said to be present when there was edema of the mucosa, a greater infiltration of lymphocytes than in the minimal lesion and some muscular thickening. *Chronic fibrous cholecystitis* was the term applied to those gall-bladders with markedly thickened walls, cuboidal epithelium that often is absent in places, and diverticular crypts. This type of lesion is almost always accompanied by biliary calculi.

TABLE I  
IMPORTANCE OF PATHOLOGIC CHANGES TO PROGNOSIS  
AFTER CHOLECYSTECTOMY

	Well	Improved	Unimproved	Post-operative Death	Total
Minimal lesion	11	22	21	3	57
Cholesterosis	14	2	14	1	31
Chronic catarrhal cholecystitis	18	16	13	4	51
Chronic fibrous cholecystitis	2	3	0	0	5
Cholesterosis with stone	6	11	0	0	17
	51 or 31.7 per cent	54 or 33.5 per cent			161

Another angle from which this study has been made has been to attempt to correlate the cholecystographic examinations with the ultimate results in cases of the stoneless gall-bladder. Of the 161 cases that have been made the basis of this whole study, for various reasons only 114 are available for a particular investigation of the correlation of the cholecystographic response with the ultimate postoperative results. These are presented in Table II.

TABLE II  
CHOLECYSTOGRAM AND PROGNOSIS—114 CASES

Type of Cholecystographic Response	Total	Clinical Result				Percentage Well or Improved
		Well	Improved	Unimproved	Post-operative Death	
Normal gall-bladder	10	5	1	4	0	60
Deformed shadow	8	4	2	2	0	75
Faint shadow	75	22	22	28	3	59
No shadow	21	6	7	5	3	62
	114	37	32	39	6	60

Certain rather astonishing results have been obtained from this particular study. It will be seen, for example, that the total percentage of well or improved patients, which is 60, is about the same as the percentage that showed a faint shadow or a shadow which was designated as being normal. Some discussion is needed to clarify these points. The 10 patients who were operated on in spite of a normal cholecystographic response, the operation was done because it was

felt that the symptoms warranted the operation in spite of the negative x-ray examinations. The series of 10 cases of this sort is, of course, far too small from which to draw any sweeping conclusions. Moreover, since 6 of the patients considered themselves either well or improved after operation, the authors are inclined to assume that probably the removal of the gall-bladder had little or nothing to do with the relief of the symptoms. The routine procedure used by Graham and Mackey (*Ibid*) is to remove the appendix also whenever a cholecystectomy is performed. It is within the range of possibility, therefore, that the removal of a diseased appendix was perhaps more responsible for the relief of symptoms in these cases than the removal of a normal gall-bladder.

This study emphasizes the point that from the standpoint of satisfactory results, the symptom of *pain*, particularly the typical biliary colic, is an important feature. In the absence of severe pain the beneficial results to be obtained by cholecystectomy in cases of a stoneless gall-bladder are likely to be unsatisfactory in approximately 40 per cent. There seems at present to be little justification for the subjection to operation of patients who have only the early beginnings of cholecystic disease, unless one is interested in the prevention of complications. At any rate, the evidence indicates that if such patients are operated upon, the results will be far from satisfactory in almost one-half of the cases. In this article no particular mention has been made of other features of cholecystic disease, such as *flatulent dyspepsia*. It will be apparent, however, from the remarks already made that symptoms other than pain which are commonly associated with gall-bladder disease are much less likely to disappear after cholecystectomy than is pain itself, unless the changes in the organ are definite and marked. The determination of how much a patient's symptoms are due to the gall-bladder in a case of minimal disease of that organ is extremely difficult. Many of these patients are undoubtedly on the borderline between purely functional and anatomic disorders that produce disturbances of function. In order to arrive at a satisfactory incrimination of the gall-bladder, it is necessary to examine the patient thoroughly with reference to the possibility of other sources of the complaints; and so far as the gall-bladder itself is concerned, it is necessary not only to take a very careful clinical history, but also to resort to various special methods of examination. Even after the presence of cholecystic disease is demonstrated in the anatomic sense, however, it is still difficult to be satisfied that the function of the organ is sufficiently disturbed by those pathologic changes to cause the symptoms of which the patient complains. The presence of calculi and the history of typical biliary colic greatly increase the chance of a satisfactory result after cholecystectomy.

**HERNIA.**—*Etiology.*—*Relation of Trauma*—According to J. J. Moorhead (New England J. Med. 209: 568 (Sept. 21) 1933), hernia is never caused by injury, its development is always preceded by a preformed sac. Hernia, however, may be aggravated by injury. Immediate disabling pain is the chief *symptom*. This is associated with nausea, tenderness, swelling and other manifestations. Operation usually discloses extrasaccular and intrasaccular adhesions, indicating that the process is old. Pathological examination of the sac demon-



strates chronic peritonitis and fibrosis. Hernia is usually a chronic progressive condition, a ptosis, a diverticulum. It is rarely an acute surgical entity. A large proportion of males have hernia without its being recognized. Surgeons are also unaware of it when treating for contiguous injury grave enough to cause aggravation of the hernia. Herniæ are subject to periods of augmentation and remission.

**DIAPHRAGMATIC HERNIA.**—In discussing this subject, C. A. Hedblom (Ann. Int. Med. 8:156 (Aug.) 1934), states that diaphragmatic hernia may be present at birth, may be acquired through anatomically weak areas, or may result from direct injury to the diaphragm or a sudden accidental marked increase in the intraabdominal pressure. The *cause* of the congenital type of diaphragmatic hernia is not definitely known. That of the acquired type is chiefly increased intraabdominal pressure in the presence of congenital weakness of the diaphragm or an acquired weakness due to atrophy of muscle and absorption of the fat deposit in the anatomical foramina.

The *symptoms* of diaphragmatic hernia are referable to the thorax or abdomen, or both, in varying proportions. The thoracic symptoms are due largely to interference with the functions of respiration or circulation, or both. Abdominal symptoms are largely attributed to a greater or less degree of obstruction of the stomach or intestines. The *physical findings* are chiefly thoracic. Borborygmi, partial dextrocardia, and variable physical findings occurring with changes in position are particularly significant. The *diagnosis* is confirmed by the demonstration of an abdominal viscus above the diaphragm, except in cases of hiatus hernia. The *treatment* of small, reducible, symptomless hernia at the esophageal hiatus is **expectant**. All other types are repaired **surgically**. The most serious *complication* is intestinal obstruction.

**Complications.**—A. V. Bock, J. W. Dulin, and P. A. Brooke (New England J. Med. 209:615 (Sept. 28) 1933) review 10 cases of hernia of the stomach through the esophageal orifice of the diaphragm, associated with *bleeding from the gastrointestinal tract*. In no case were they able to detect any other cause for the bleeding by clinical or x-ray methods. In 3 cases abdominal exploration failed to reveal any other cause. In the 2 cases that came to autopsy, small injected areas were found in the mucosa of the prolapsed portion of the stomach. The authors believe that the cause of the bleeding was congestion of the gastric mucosa due to venous pressure.

**Diagnosis.**—Early gastric pain relieved by lying down and associated with paradoxical dysphagia and a cardiopulmonary syndrome caused by a full stomach and relieved by the frequent and copious vomiting of mucus accompanied by a rhythmical gurgling which is synchronous with respiratory or cardiac movements, are signs indicating x-ray examination, the only means by which a definite diagnosis can be made, according to F. Trémolières, A. Tardieu, and G. Caquot (Presse méd. 42:292 (Feb. 21) 1934).

**CONGENITAL DIAPHRAGMATIC HERNIA.**—G. Bignami (Radiol. med. 20:1351 (Nov.) 1933) reports the case of a male infant 10 days old with respiratory, circulatory and digestive disturbances. Normal delivery was followed immediately by dyspnea of the stenotic type, with intervals of suffocation which resulted in cyanosis, and by vomiting which resulted in malnutrition and marked

loss of weight. The thorax was greatly expanded, almost in the position of forced inspiration, while the abdomen was scaphoid so that the division between the thorax and abdomen was almost precipitous. X-ray examination revealed a shifting of the mediastinal shadow to the right and a marked and irregular transparency of the left pulmonary field without definite signs of lung structure. A barium meal demonstrated the presence of intestinal loops in the left pleural cavity.

**HIATUS HERNIA.**—A. Wagner (Hospitaltid. 76:257 (Mar. 9) 1933) states that the formation is favored by all conditions causing an increase of the intraabdominal pressure, such as obstipation, pregnancy, prostatic hypertrophy, long-continued bodily exertion, trauma, chronic cough, ascites and loss of fat and muscle tissue. Less common predisposing causes are scarring of the esophagus, which pulls the stomach up into the thorax, and congenital defects. Among the most common *symptoms* is pain. This is usually localized in the region of the upper epigastrium and occurs before, during or after meals, or periodically. It may be provoked or relieved by changes of position. Dysphagia is a less common but important symptom. Other symptoms are belching, pyrosis, vomiting, nausea, hematemesis, occult hemorrhages and melena. In the *differential diagnosis* it is necessary to rule out epiphrenic and subphrenic esophageal diverticula, a cardiac antrum of the esophagus, cardiospasm, other diaphragmatic herniæ, relaxation of the diaphragm in the region of the esophageal hiatus, and diverticulum of the stomach. The patient should be examined in the standing and reclining positions. Fluoroscopy after an opaque meal is recommended.

**INTESTINES.—CHRONIC CICATRIZING ENTERITIS.**—F. I. Harris, G. H. Bell and H. Brunn (Surg. Gynec. Obst. 57:637 (Nov.) 1933) point out that Crohn, Oppenheimer and Ginzburg have described a surgical disease which they call "*regional ileitis*." This disease has well-defined clinical and pathologic characteristics and its description will be found to cover many of the heretofore unclassified inflammatory tumors and lesions of the small intestine. The authors report 3 cases of the disease, in one of which the jejunum was found to be involved. They suggest the name "chronic cicatrizing enteritis" as a more descriptive and inclusive term for this new surgical entity. Medical treatment is symptomatic and supportive. A complete cure must depend on the surgical resection of the diseased intestine. In cases in which this has been done successfully, the patient has been restored to complete health. Such a case may require multiple stage operations. In the authors' experience a preliminary short-circuiting operation, such as **ileocolostomy**, with a later **resection of the diseased intestine** when the patient has been built up, would seem to be the better surgical judgment. Simple ileocolostomy without the removal, either at the original operation or later, of the diseased obstructed intestine carries with it the added danger of the obstructed intestine becoming dilated and ulcerated. The recent work of Holm has definitely shown both experimentally and clinically that the sidetracked intestine in short-circuiting operations is a constant menace to the health of the patient. Berg advocates resection with ileocolostomy as the operation of choice.

**COLON.—ABNORMALITIES.**—The clinical significance of *variations in fixation of the cecocolon* is outlined by J. L. Kantor and S. Schechter (Am. J. Roentgenol 31.751 (June) 1934). The authors believe that there is no need for operative intervention in atypical fixations of the colon except when actual evidence of intestinal obstruction is demonstrable. This would practically restrict such intervention to cases of volvulus and intussusception when excessive mobility is present and to cases of obstruction by bands when excessive fixation is present. The observation that *hepatic flexure fixation* is not associated with either gall-bladder disease or gall-bladder operations may be explained by the fact that in the majority of instances the fixation represents a congenital and not an acquired phenomenon. Similarly, the majority of cecal fixations may also be regarded as congenital rather than acquired in origin. The average vertical range of mobility of the hepatic flexure is  $1\frac{2}{3}$  inches. Normal variations in mobility range from more than 1 inch to less than 3 inches. The average vertical range of mobility of the cecum is  $1\frac{1}{3}$  inches. Normal variations range from 1 to  $2\frac{1}{2}$  inches. *Hypermobility of the hepatic flexure* may be said to exist when the vertical range is 1 inch or less. *Hypermobility of the cecum* may be said to exist when the vertical range is  $2\frac{1}{2}$  inches or more, and *hyperfixation* when the vertical range is 1 inch or less. The authors' study does not appear to reveal any marked clinical disturbances associated with the usual ranges of variations in fixation of the cecocolon as a whole, or of either of its terminations regarded separately. Such disturbances as are present seem to be adequately handled by the usual methods of conservative medical management, such as are implied in the competent treatment of the unstable colon. In none of their cases did the authors recommend surgical therapy.

**CARCINOMA OF COLON.**—Multiple primary malignant growths, according to A. J. Cokkims (Brit J Surg 21.570 (Apr) 1934), occur more frequently than can be explained by mere coincidence. While they may be attributed to the presence of multiple or diffuse precancerous lesions, a more probable cause is increased susceptibility to malignant disease. One growth does not confer immunity to the development of another.

The etiology of multiple carcinomata of the intestine is the same as that of multiple primary growths elsewhere. Multiple adenomata are definite causes of multiple cancers of the colon and rectum.

All forms of intestinal polypi are potentially malignant and should be treated as potentially malignant growths.

The possibility that more than one growth may be present or develop should be remembered in all operations for cancer of the intestine and in the prognosis of that condition.

**Symptoms and Diagnosis.**—D. P. D. Wilkie (Lancet 1.65 (Jan 13) 1934) reports on 101 cases of carcinoma of the colon in which he was able to perform a **partial colectomy**. In 74, the lesion was in the distal half of the colon, i. e., beyond the midpoint of the transverse colon; in 27 it was in the proximal half. The sites were as follows: pelvic colon, 51 cases; ascending colon, 15 cases; descending colon, 13 cases; transverse colon, 11 cases; cecum, 5 cases; splenic flexure, 5 cases; and hepatic flexure, 1 case.

In its early stages, cancer of the colon may produce few symptoms. If it is low down in the pelvic colon, it may cause occasional tenesmus, the passage of blood and mucus, and some slight irregularity of the action of the bowel. A growth in the distal part of the colon is usually not associated with an appreciable loss of weight. In cases allowed to progress until complete obstruction has developed, the most striking feature on examination may be swelling and tenderness in the lower right quadrant of the abdomen

C. Crawford (*Acta chir. Scandinav.* 74:513, 1934) bases his report on 161 cases of cancer of the colon. In 126 cases radical operation was done with a primary mortality of 35 per cent. In 5 cases, death occurred soon after a preliminary operation for the relief of ileus. Thirty cases were inoperable.

A good therapeutic result requires early diagnosis. Therefore, a knowledge of the initial symptoms is essential. The author divides these into the following 7 groups:

1. Generalized, diffuse abdominal symptoms. These were present in 101 of the cases reviewed and were initial symptoms in 83

2. Symptoms of intermittent ileus. These occurred in 60 cases and were initial symptoms in 20

3. Acute ileus. This occurred in 102 of the cases and was an initial symptom in 16

4. Emaciation and debility. These occurred in 82 of the cases reviewed and were initial symptoms in 13

5. The admixture of blood and mucus in the feces. This occurred in 26 cases and was an initial symptom in 6

6. Constipation. This was present in 51 cases and was an initial symptom in 16.

7. Diarrhea. This occurred in 29 cases and was an initial symptom in 6.

The average length of time between the occurrence of the initial symptoms and the diagnosis in the majority of cases is 7 months, due to the fact that persons of cancer age are not sufficiently aware of the importance of submitting to examination for vague symptoms

The author emphasizes the value of x-ray examination in the diagnosis of all uncertain cases and in the planning of the operation

**Prognosis.**—A factor of very great importance in the primary mortality, according to Crawford (*Ibid*), is the time at which the radical operation is undertaken. It is not sufficient merely to relieve the ileus. Patients without ileus as well as those with this condition must be given sufficiently prolonged preliminary treatment to increase their resistance and reduce the pathogenicity of the intestinal flora. The author believes that in 50 of the cases reviewed the preliminary treatment was satisfactory. While 7 (14 per cent) of the 50 patients died, the death of only 2 (4 per cent) could be referred to the operative method. Of the remaining 71 patients treated by resection, 24 (34 per cent) succumbed as the direct result of the operation

**Treatment.**—Some indications for surgical treatment of carcinoma of the colon are outlined by D. P. D. Wilkie (*loc cit*). He states that in the past few years radiotherapy has been substituted for radical operative measures for cancer

of such regions as the lip, tongue, mouth, cervix, and breast. In cancer of the hollow viscera of the abdomen, however, operation is still the only means of cure. In cases of malignant tumors of the colon, which are common, the growth of the lesion is usually slow and lymphatic involvement occurs relatively late.

When the patient is seen first after acute obstruction had developed, the immediate indication is drainage of the bowel above the obstruction by **cecostomy**. For free drainage the cecum must be brought to the surface and a tube of adequate size introduced. As tumors of the colon grow slowly, extirpation of the growth should be delayed for several weeks after the cecostomy.

The chief danger of **resection** of the colon is infection due to imperfect technic, inadequate preparation, or leakage at the suture line.

The author attempts immunization by giving **injections of bacillus coli** and **streptococcus** 8 and 3 days before the operation. To produce a leukocytosis on the morning of the operation, he gives an intramuscular injection of 5 c.c. of a 5 per cent. solution of **nucleinate of soda** the evening before.

The *technic* should include complete mobilization of the involved portion of the colon so that the ends to be sutured will fall together without tension. If **end-to-end anastomosis** is decided upon, the taenia of the colon must be divided to get rid of the sacculations so that tension will be equal on all points of the circumference of the bowel. Interference with the blood supply of the approximated cut margins must be avoided as far as possible. If not already established, a **cecostomy** opening should be made to prevent gaseous distention of the colon during the first week after the operation.

**DIVERTICULA OF DUODENUM AND JEJUNUM.**—H. C. Edwards (Lancet 1:169 (Jan. 27) 1934) defines the primary acquired diverticulum of the *duodenum* as a "thin-walled sac opening from the concave surface of the bowel at the point corresponding to the penetration of the wall by a biliary or pancreatic duct or by a blood-vessel." In each of the author's 5 cases the fundus of the diverticulum was devoid of a true muscular coat, but otherwise there was no abnormality of the sac wall. The most common situation of duodenal diverticula is the second portion of the duodenum.

Next to the duodenum, the most common site of primary acquired diverticula in the small intestine is the *jejunum*, where they may be single or multiple. The smaller diverticula lie to one side of the mesentery, the opening in the bowel being lateral to the line of mesenteric attachment. In the author's experience every small diverticulum is paired, its fellow being situated equidistant from the mesentery on the opposite side. Edwards attributes the large pouches often found to fusion of a pair of smaller ones. According to his observations, the site of origin of these diverticula is not at the line of attachment of the mesentery, but to one or the other side of it, exactly at the point of entrance of the blood-vessels. Microscopic examination of such diverticula shows an artery and vein at the fundus. This finding with an otherwise normal picture (except for the lack of a muscular coat) is taken as evidence that the pouches are hernias of mucous membrane through the muscular coats at points weakened by the penetration of blood-vessels.

The presence of a weak area in the bowel wall and a pulsion force from within the bowel, therefore, can account for the formation of diverticula. Although several other theories have been advanced with regard to the cause of weakness of the wall, the author believes that the most logical theory is that which takes into account the penetration of the vessels. The pressure within the bowel depends on 2 factors, *i. e.*, the contents and the muscular contractions. Abnormally high pressures may occur in the duodenum under certain circumstances, the condition of the pylorus being a definite factor. In the jejunum it is necessary to postulate some irregularity in muscular action to explain increased pressure in the lumen.

**Diagnosis.**—According to Edwards (*Ibid.*), the symptoms of duodenal diverticula are not sufficiently distinctive to allow a clinical diagnosis with any degree of certainty. The only reliable method of diagnosis is x-ray examination. Great care must be exercised in attributing various vague digestive disturbances to diverticula discovered by x-ray examination, because the presence of diverticula does not necessarily mean that they are causing symptoms. Hence, complete gastrointestinal studies to rule out all other possibilities, including disease of the gall-bladder, must be made. Only when x-ray examination shows barium retention in a diverticulum over a long period of time, is it justifiable to conclude that the diverticulum is the cause of symptoms. Diverticula of the jejunum rarely cause symptoms unless they are complicated by infection, perforation, or obstruction.

**X-ray Diagnosis**—C. D. Costello (*Brit J Radiol* 6:577 (Oct.) 1933) reports 6 cases in which the diagnosis was made by x-ray examination and presents the following diagnostic observations:

1. The shadow of the diverticulum is distinct from that of the duodenum and is usually round and smooth in filling and outline.
2. Under the fluoroscope, a connection can usually be demonstrated between the two structures by emptying the diverticulum into the duodenum by palpation.
3. Barium is often retained in the diverticulum for several days after the duodenum has been emptied.
4. Tenderness over the diverticulum on fluoroscopy should suggest the diagnosis of diverticulitis or peridiverticulitis.

The author states that frequently the lesions will be missed on fluoroscopic examination unless adequate care is exercised in inspecting the second, third, and fourth portions of the duodenum with the patient in the erect and recumbent positions.

**Treatment.**—Edwards (*loc cit*) advocates the removal of duodenal diverticula which are causing symptoms. The operation is a serious one. Removal of the sac and repair of the duodenal wall are sufficient. In multiple jejunal diverticula, resection of the affected gut is the only treatment possible.

**DIVERTICULA, JEJUNOILEAL.**—**Classification.**—I. Fraser (*Brit J. Surg* 21:183 (Oct.) 1933) suggests the following classification of jejunoileal diverticula: (1) anomalous, in general of the traction type secondary to some other abdominal condition; (2) enterogenous, congenital in origin, arising primarily as isolated masses of cells which separate from the primitive gut and become vacuolated, forming cysts which later become attached to the intestine.

to produce diverticula, (3) Meckel's diverticulum, arising from the unobliterated vitellogastrointestinal canal to assume numerous clinical forms, and (4) multiple false diverticula, a rare acquired condition, the frequency of which, because of the absence of symptoms in most cases, will never be known

*Multiple false diverticula* may occur anywhere between the duodenojejunal angle and the ileum. They appear as thin-walled sacs arising from the mesenteric border of the gut and vary in size from that of a pea to that of an orange. As many as several hundred diverticula have been found in a single individual. "The origin of the sac is a projection, herniation, or protrusion of the mucous membrane at the mesenteric border of the gut through the substance of the muscle." The sacs are usually empty or contain fluid chyme mixed with air. The relatively large stoma or neck of the sac provides adequate drainage for the fluid contents and this, combined with the rapid intestinal peristalsis in the small intestine, doubtless prevents inspissation of the contents and complications such as are associated with other types of diverticula. In the late stages of the condition the size and weight of the sac may cause kinking of its neck and thus give rise to symptoms due to inadequate emptying. Microscopically, a section of the wall of the sac at the fundus shows intestinal mucous membrane covered by the peritoneum forming one of the leaves of the mesentery. Between the two there may be areolar or fibrous tissue. A fat deposit encasing the sac is common.

***Etiology and Pathogenesis.***—The condition occurs in both sexes and usually after the age of 40 years. The upper jejunum is usually affected, the larger diverticula occurring proximally. There is a definite relationship to the vasa recta. In several reported cases there was an intestinal stricture further down in the gut.

Several anatomical facts are cited by Fraser (*Ibid*) to explain the predominance of these diverticula in the jejunum. The longitudinal muscle in the upper jejunum is thinned out, wasted, or almost missing because the jejunum has a 3 times greater circumference to be covered than the ileum. This congenital divarication can be still further accentuated by separation of the mesenteric leaves by fat. The piercing of the circular tunic by the arteries and veins to the gut produces a potential site of lowered resistance. In addition, the arteries to the jejunum are larger than those to the ileum. The additional factor needed is increased pressure, such as is found in stricture of the gut, constipation, vesical straining, and coughing. It, therefore, seems evident that the causative factor is increased intestinal tension acting along the channel of the artery or at the point where the longitudinal muscle is divaricated.

***Symptoms.***—Following a report of his own case, Fraser (*Ibid*) discusses the symptoms, diagnosis, and treatment of the condition. A prominent symptom is epigastric pain or a feeling of fullness from 3 to 4 hours after meals. This discomfort is little affected by food, fluids, or alkalis, but is somewhat relieved by the recumbent position. Flatulence, borborygmi, gurgling, and rumbling are the most constant features. Melena is present in some cases. However, there is no constancy in the clinical picture. For this reason and because most cases are asymptomatic, the condition is discovered accidentally during operation for an unrelated condition or at postmortem examination.

**Treatment.**—This varies; for asymptomatic cases in which the condition is discovered clinically during routine examination, Fraser (*Ibid.*) believes that **conservative medical treatment** is indicated because most of the patients are elderly and not good operative risks and the majority pass through life without complications. In reported cases in which complications occurred, they rarely proved fatal. Fraser outlines the nonoperative treatment in detail, stressing the importance of careful follow-up examinations at 6-month intervals. In the asymptomatic case in which the condition is discovered accidentally at operation for another condition, the treatment must depend upon the judgment of the surgeon. When the patient is a relatively good operative risk, the author believes **resection of the affected gut** should be performed. He is of the opinion that operation is indicated in all cases in which the diverticula are causing symptoms, and that in such cases the procedure of choice is complete removal of the affected area with restoration of the continuity of the gut. He discusses the technical difficulties encountered in some detail. He states that only 1 case in 4 presents symptoms warranting operation.

**DIVERTICULITIS OF COLON.**—*Differential Diagnosis.*—The differentiation of diverticulitis from *carcinoma of the colon* is frequently difficult, as outlined by H. von Haberer (Zentralbl. f. Chir. 61: 805 (Apr. 7) 1934). The author reports 3 cases of diverticulitis in detail. The first was that of a woman who was subjected to operation after an erroneous diagnosis of carcinoma and even on the basis of the operative findings was believed to have a carcinoma of the sigmoid. Following the formation of a lateral artificial anus in the cecum, the fever and cachexia disappeared and the bowels moved naturally. The lesion, therefore, could not have been a carcinoma and must have been an inflammatory mass. On the basis of other observations, the author concludes that the condition was probably diverticulitis.

In the second case reported, the correct diagnosis was made before operation. Perforation of the bladder had occurred with grave sequelæ, but cancer cachexia was absent and x-ray examination showed a pronounced diverticulum formation in the region of the stenosis.

The assumption that because of the extensive adhesions caused by diverticulitis, practically no other *treatment* than colostomy is possible, has been proved incorrect by the success of **resection** done in 2 stages. An anastomosis to pass around the obstruction is usually impossible or too dangerous because of the extensive adhesions of the inflammatory tumor and the pathological changes in the walls of the intestine above and below the mass. On the other hand, the inflammatory tumor may be removed from above, despite the adhesions, in fact, such removal may be necessary as, for example, in cases in which there is perforation of the bladder, with resulting cystitis and danger of ascending infection. In such cases, the only procedure possible is separation of the inflamed intestinal mass from the bladder, followed by suture of the bladder. A threatening infection of the peritoneum is best prevented by extraabdominal delivery and fixation or removal of the involved portion of intestine. The author obtained good results from removal. He concludes that the lateral artificial anus should not be closed within less than a year, because in the second case he reports the pouch of



Douglas drained pus for a very long time and subsequent x-ray examination with the use of a contrast medium disclosed the presence of other diverticula in the lower part of the colon.

The inflammatory tumor of the colon invaded the posterior wall of the bladder also in the third case reported by von Haberer, but in this instance the mucosa was not perforated and at operation could be preserved intact. As the patient was corpulent and the mesentery markedly shrunken, exteriorization of the diseased portion of intestine could not be considered. Resection with end-to-end anastomosis of the intestine was technically possible, but was believed to be contraindicated because of the presence of inflammatory changes throughout the entire descending colon. Therefore, only the **mass adherent to the bladder** was **removed** and an **artificial anus** was established. The patient made a remarkable recovery. Later, restoration of normal conditions may be possible.

A case of true diverticulum of the *sigmoid* is reported by J. N. Coombs (S. Clin. North America 14: 169 (Feb.) 1934) which caused intestinal obstruction necessitating an emergency **cecostomy**, giving relief from the obstruction. One month later exploration of the abdomen revealed a hard annular mass, thought to be *carcinoma*, adherent to the left lateral wall of the pelvis. A one-stage **Balcock proctosigmoidectomy** was done. Examination of the specimen showed a large indurated area on the concave side of the colon about 25 cm. above the anus which nearly surrounded the bowel. This area was 5 cm. in diameter and very hard. When the bowel was incised, an opening was disclosed 1 cm. in diameter, admitting a probe. It was a complete diverticulum.

In reviewing this case it is significant that the cecostomy closed spontaneously and also that the mass, felt on vaginal examination at the time of the patient's first admission, was not palpable at the time of her second admission.

It is apparent that, with the relief of obstruction by cecostomy, the occluding inflammatory swelling subsided sufficiently to allow the channel to almost reach a normal condition.

The similarity, on examination, of this case of diverticulitis and that of a malignant tumor was so marked as to cause confusion in diagnosis.

It is evident that even at operation it may occasionally be impossible to distinguish a diverticulitis causing obstruction from a carcinoma until microscopical section clears away the doubt. Rankin mentions that a relatively long segment of the colon is involved in diverticulitis, whereas carcinoma usually involves a much shorter segment. Exceptions, however, occur as in this case.

When the growth can be reached by the proctoscope, the absence of involvement of the mucosa indicates that the condition is probably not cancerous. J. F. Erdmann (J. A. M. A. 99: 1125 (Oct.) 1932) emphasizes the fact that the mucosa of the colon is rarely involved in diverticulitis. The obverse obtains in malignant conditions. Erdmann also mentions that he can think of no more difficult bit of work than seeing through a proctoscope the openings of any of these diverticula, yet can conceive of the accidental exposure of a relatively small opening.

The x-rays may be of great assistance in the diagnosis after subsidence of obstructive symptoms, particularly in outlining multiple diverticula.

In the presence of intestinal obstruction, the differential diagnosis between diverticulitis, producing intestinal obstruction, and *carcinoma of the sigmoid* may be difficult. With the relief of obstruction and recovery of the patient, curative treatment is then to be considered. In the presence of diverticulitis, conservatism may be followed, although recurring attacks of partial or complete obstruction may take place, requiring later resection.

When doubt exists as to whether the process is of a malignant nature or not, **excision** of the involved segment of the colon may be desirable. The Babcock one-stage **proctosigmoidectomy** with the formation of a **perineal anus** enables the operator to remove the lower sigmoid for diverticulitis without peritoneal contamination and with a functional anal opening.

**DUODENUM. — DUODENAL ULCER. — Occurrence.** — The multiplicity of duodenal ulcerations is commented upon by E. Just (Arch. f. klin. Chir. 179 211 (Mar 15) 1934). In a consecutive series of 60 cases operated on for duodenal ulcer, the author opened the lumen of the duodenum and carefully inspected the duodenal mucosa. He found that the incidence of multiple ulcerations and corresponding multiplicity of pathologic states is greater than was formerly believed. Twin ulcers ("kissing ulcers" of Moynihan) were observed in 46, or 76 per cent, of the cases. Scars in the vicinity of ulcers were found in 8 cases. These were radiating or star-like. In the remainder of the cases the author found large ulcerations involving both the anterior and the posterior wall. These, he believes, were the result of coalition of an anterior and a posterior wall ulceration. Consideration of this group of cases suggests that multiplicity of lesions is present in 100 per cent. of all cases of duodenal ulceration. These observations lend support to von Haberer's opinion that recurrent ulcers after gastric resection are overlooked ulcers. While observations on so small a group of cases do not rule out the existence of a single duodenal ulcer, they emphasize the great frequency of multiple lesions and the necessity for awareness of this fact on the part of the surgeon.

**Hemorrhage.** — From a review of 1804 cases, A. W. Allen and E. B. Benedict (Ann Surg 98 736 (Oct) 1933) believe that patients suffering from duodenal ulcer who have recovered from a severe hemorrhage should be subjected to surgery in a quiescent state, as the possibility of a persistence of symptoms is great and the incidence of future episodes of severe hemorrhage is about 40 per cent. Spontaneous recovery is less likely with increasing age. About one-third of all duodenal ulcer patients requiring hospitalization, observed by the writers, had gross bleeding. More than 3 per cent died of hemorrhage. The mortality in sudden massive bleeding from duodenal ulcer was 14.5 per cent, regardless of treatment. Age seems to be the most striking single factor in determining the possibility of spontaneous recovery. Death from hemorrhage occurs rarely in patients less than 50 years of age.

In persons with acute massive hemorrhage beyond middle age and who do not show early evidence of a complete cessation of bleeding, **immediate surgery** should be contemplated. Matched citrated blood should be kept in the refrigerator, or a donor should stay at the hospital. **Transfusion** should be done quickly if there is a second collapse and before the systolic pressure falls below 70 mm. of

mercury. If there is a rapid loss of the benefits of this transfusion, a large transfusion should be given and the patient immediately operated on.

The authors describe an **operation** for patients who continue to bleed owing to a large open vessel situated in an eroded area in the pancreas, as follows:

In order to control the loss of blood during the operative procedure, the lower third of the stomach down to the ulcer is transected and freed. Then the distal clamp is removed and the anterior wall of the lower segment is opened. The bleeding point is controlled by a finger or tamponade and the resection continued without serious loss of blood. The vessels entering the edge of the ulcer are intercepted as the inflammatory tissue is cut across. When the hemorrhage is controlled, a retractor is placed in the duodenum and the level of the ampulla of Vater is ascertained. If there is room to free the duodenum beyond the bed of the ulcer and to allow a satisfactory turn-in, the operation is easily completed. If there is doubt concerning this, or if the erosion in the pancreas is large and sufficiently deep to have opened an accessory pancreatic duct, a modified procedure is done. A part of the elevated distal portion of the stomach is eliminated, leaving a sufficient amount of the prepyloric region for easy suture. The duodenum and the stump of the stomach are sutured in such a way as to enclose the ulcerated area in the pancreas. If it is advisable to destroy the remaining activating area in the antrum and the patient's condition permits, the mucosa is removed from this region, as suggested by Bancroft, before the closure is made. Anastomosis between the stomach and the intestine may be made by the Polya or second method of Billroth.

A case of coincident *hemorrhage and perforation* in chronic duodenal ulcer is reported by J. Burke and C. Kummer (*Am. J. Surg.* 22:274 (Nov.) 1933). They conclude, after a review of the literature, that the coincidence is rare. The patient, after a massive hemorrhage, was admitted to the hospital in a desperate condition. Despite blood transfusion and supportive treatment, the patient died. An autopsy showed the peritoneal cavity to be filled with turbid purulent fluid. The intestines were injected and matted together by exudate. A perforation 1.5 cm. in diameter was seen just distal to the pylorus on the anterior surface of the duodenum. Its upper border was at the pyloric ring. A small artery plugged by a recent thrombus presented at the bottom of the crater, arising from the distal wall of the ulcer. There was marked callous induration surrounding the perforation. No other gastric lesions were found other than a mild gastritis involving the antrum. The kidneys were typically arteriosclerotic, and the arteries throughout the entire body were like pipestems in consistency.

The authors comment that at the time of admission, operation was considered and deferred in the presence of active hemorrhage. At no time did the patient's condition improve sufficiently to encourage operative therapy. They state, however, that if they had interpreted back and shoulder pains as indicative of approaching perforation, the risk would have been undertaken. The accepted opinion concerning the rarity of perforation with acute hemorrhage, together with the relative lack of physical signs put the authors off guard until it was too late.

**Operations for Duodenal Ulcer.**—Experimental exclusion operations were used on 2 series of animals by M. E. Steinberg (*Ibid.*, 23:137 (Jan.) 1934). Of the first series (23 animals), 21 survived. These animals had a typical Finsterer modification of the second Billroth stomach resection, with an Exalto shortcircuiting operation and removal of the motor part of the stomach. Seven animals, in addition to the foregoing procedure, were subjected to a kink distal to the anastomosis. None of the 23 animals developed an ulcer. In the second

series of animals a typical Devine operation was performed with an Exalto short-circuiting of the duodenal contents, the motor part of the stomach being left in place. There were 12 dogs in this series, and 6 developed definite large chronic ulcers. The von Eiselsberg operation should be abandoned. There is not sufficient clinical evidence to justify a definite expression of opinion on the results of the Devine exclusion operation. From the experimental work and theoretical and anatomic considerations, this operation should influence the production of jejunal ulcers. The author's personal clinical experience in 12 cases with a typical **Finsterer exclusion operation** has been favorable.

The value of **circular resection** in chronic gastric or duodenal ulcer is discussed in a monograph by K. Roholm (*Acta chir. Scandinav.* 73: 433, 1934). He first outlines the objectives of surgical treatment of these conditions—the correction of the pathological process or its associated complications. The surgeon corrects mechanical malfunction, such as that due to stenosis, removes either the ulcer and a greater or smaller part of the adjacent tissue, changes gastric function by decreasing the emptying time of the stomach and neutralizing the gastric contents or decreasing gastric secretion so that the gastric load is diminished, or changes the site of gastric emptying so that mechanical irritation of the ulcer is reduced.

The author next discusses the *principles* of the different surgical technics, reviews the physiology of the stomach and duodenum, and traces the historical development of ulcer surgery.

The type of lesion, the duration of the symptoms before surgery, the indications for operation, the type of surgery used, the age of the patient, and the operative mortality in the cases reviewed are tabulated. The results are divided into 4 groups: (1) complete cure, (2) almost complete cure; (3) improvement, and (4) poor results.

In the 130 cases reviewed, the operations included 40 circular or sleeve resections of the gastric corpus and 90 pylorotomies, *i. e.*, removal of the pylorus and a portion of the antrum and the first part of the duodenum. In addition, there were 8 cases of radical surgery secondary to a gastroduodenal operation.

In the 122 primary operations the immediate surgical mortality was 10.7 per cent (13 deaths), and in the 8 cases of secondary resection it was 37.5 per cent (3 deaths). The cause of death was bronchopneumonia in 5 cases, an unknown cause or a combination of factors in 3 cases, a questionable error of surgical technic in 2 cases; peritonitis in 2 cases; and pulmonary embolus in 1 case.

In 105 cases the patient was subsequently reexamined and the *result of the operation* evaluated. Sleeve resection of the gastric corpus was abandoned because of frequent ulcer formation at the site of the operative scar. Primary resection of the pylorus was followed by improvement in 81.5 per cent of the cases and by unsatisfactory results in 18.5 per cent. The mortality of this operation was 12.2 per cent. From a comparison of these results with those obtained in the 101 cases in which gastroenterostomy was done in the same clinic in the period from 1906 to 1916, the author concludes that there was no definite difference in the results of these 2 types of surgery when they were employed routinely.

**DUODENAL STASIS.**—In the opinion of E. H. Pool, W. L. Niles and K. A. Martin (Ann. Surg 98:587 (Oct.) 1933), chronic duodenal stasis and its surgical treatment have not been given proper consideration by the majority of clinicians. Stasis in the duodenum may cause serious and prolonged symptoms leading to chronic invalidism, but may be corrected by timely surgery. It may be brought about by fixation, distortion, or compression of the first or second portion of the duodenum by bands or adhesions, notably by extension of the hepatoduodenal ligament. There may be a temporary loss of tone, with impairment of the function of the duodenum or obstruction at or near the duodenojejunal junction.

**Symptoms and Diagnosis.**—The patient complains of indigestion of varying degrees of severity with a sensation of weight in the epigastrium soon after meals which is often attributed to gas on the stomach, but is not relieved by belching. Some patients have epigastric distention and soreness beneath the manubrium sterni. Nausea is a common symptom, and pain is often very severe. The pain is frequently mistaken for biliary colic and may require morphia. The pain and vomiting may last for several hours or days, and may suggest acute intestinal obstruction. Some patients are relieved by the recumbent or knee-chest position. Headaches and faintness are common. The symptoms may have persisted over a number of years or may have developed very suddenly. The condition occurs most frequently in persons of the hyposthenic type and visceropotosis may be revealed by x-ray examination. The fluoroscopic examination of the duodenum necessary for diagnosis demands expert technic.

**Treatment.**—It is emphasized by Pool and his associates (*Ibid*) that it is neither wise nor necessary to operate on all patients with duodenal stasis. The decision as to operation requires careful thought and consideration of the patient's nervous and psychic status. Operation should not be undertaken before a careful medical régime has been tried and has failed to relieve the symptoms. It has been commonly noted that the only cases helped by medical treatment are those with a short history of indigestion and very moderate stasis.

The **surgical treatment** usually consists in the freeing of bands or constricting adhesions. For obstruction at the terminal portion of the duodenum, **duodenojejunostomy** is indicated. This operation is safe and gives good results.

In a period of 9 years Pool has operated on 11 carefully selected cases. In 7, the result was excellent, in 2, fair, and in 2, doubtful. There were no deaths.

**PERIDUODENITIS.**—Periduodenitis of *appendicular origin* is more frequent than usually supposed. According to S. Kadrnka and P. Bardet (Arch. d. mal. de l'app. Digestif 24:354 (Apr.) 1934), it is more frequent, in fact, than postcalculous or postulcerous periduodenitis and is generally found in young adults. So-called essential periduodenitis must be considered only after the exclusion of disorders both near and far, and especially appendicitis, even when apparently clinically cured. In such instances, histologic evidence of the remains of an old appendicitis is necessary. Periduodenitis of appendicular origin generally involves the proximal part of the first portion of the duodenum and by choice the lesser curvature of the bulb. It is also frequently localized at the end of the

third part in the region of the neck of the mesentery, thus producing a mesocolic form, which is characterized by a nonreducible stenosis. In practice, appendicular periduodenitis forms 2 groups: (1) that in which the dyspepsia is accompanied by the appendicular syndrome, and (2) that in which it is not. In the first form, the x-rays are largely responsible for the pathologic diagnosis. In the second group, clinical diagnosis is especially difficult.

**Treatment.**—The authors consider that treatment should be directed both toward operative **freeing of the duodenal adhesions** and **removing** of the primary focus, *i. e.*, the **appendix**. Although good results sometimes follow appendectomy alone, a second operation is often necessary, and it seems desirable to perform the two procedures at the same time rather than run the risk of a second operation. They conclude that, in view of the numerous early and late complications of appendicitis, it is wise to remove this organ at the first sign of involvement and even better to remove a normal appendix than chance the complications of which periduodenitis is only one.

**SARCOMA OF DUODENUM.**—A *leiomyosarcoma* of the duodenum is reported by D H Andersen and F Doob (Arch. Path 16:795 (Dec.) 1933), with symptoms referable to repeated hemorrhage into the intestine for 5 years, compression of the inferior vena cava for 7 weeks and a palpable tumor in the right side of the abdomen for 6 weeks. The tumor compressed the inferior vena cava, and thrombi were formed in the common iliac veins. Death resulted from pulmonary embolism. The authors analyze this case and the 18 additional cases of leiomyosarcoma of the small intestine reported in the literature.

C. S. Williamson (West J Surg 42 207 (Apr) 1934) cites a case of primary *sarcoma* of the duodenum in which the tumor started as a fibroma of the duodenum and underwent malignant degeneration. The diagnosis of a duodenal tumor was made during the course of an exploratory laparotomy. A **preliminary posterior gastroenterostomy** was performed 6 months later, in anticipation of extirpating the tumor. A **partial duodenectomy** was successfully performed about 11 months after the diagnosis and the patient had an uneventful recovery. The duodenum is infrequently involved by malignant conditions, making its partial or complete resection necessary or desirable. The author believes that when such a condition exists, other factors being equal, operation should be undertaken with a reasonable hope of success, although, as in his case, it may be necessary or desirable to precede the actual attack ~~on the duodenum~~ by a preliminary gastroenterostomy. The reimplantation of the common bile duct and the major pancreatic duct into the intestine, either together or separately, can be done with a high degree of success and has been done experimentally by Mann and his coworkers. It seems that the surgeon is justified in attempting a curative type of operation for a resectable tumor of the duodenum even though it may necessitate the reimplantation of the common bile duct, the ligation of the duct of Santorini, and the reimplantation of the duct of Wirsung.

**FOREIGN BODIES.**—L H Clerf (S. Clin. North America 14 77 (Feb) 1934) states that while there is unanimity of opinion regarding the diagnosis and treatment of foreign bodies in the esophagus, there is considerable disagreement as to the proper treatment of such bodies in the stomach and intestines.

As the esophagus is part of the alimentary canal, it should always be included in the examination for a suspected foreign body in the digestive tract. The most common and often the only *symptom* produced by a foreign body in the alimentary canal is dysphagia. A foreign body in the esophagus may cause no demonstrable obstruction if only liquid food is given. The *diagnosis* can be established positively only by x-ray examination. When the foreign body is translucent, a radiopaque substance, such as barium and bismuth, either in solution or in capsule form, must be used. The *treatment* is **removal** with the esophagoscope. This is 100 per cent efficient.

Foreign bodies that enter the stomach and intestines commonly pass through the pylorus and intestinal canal. Notable exceptions are long foreign bodies such as shawl pins, needles, hair pins, nails and safety pins. These are especially prone to lodge at the duodenojejunal junction. The aid of a competent roentgenologist should be obtained to determine the size and location of the object and whether it will be able to continue its passage through the intestinal tract without interruption. If the foreign body remains in the stomach, gastroscopic removal aided by the fluoroscope is the method of choice. For cases in which foreign body has reached the intestinal tract when it is first observed, the following procedures are recommended.

1. Frequent fluoroscopic examination.
2. Continuation of the patient's usual diet.
3. The avoidance of all forms of medication that will stimulate intestinal activity.

If acute abdominal symptoms suggesting peritoneal irritation develop, surgical removal may be necessary.

The *treatment* of foreign bodies in the gastrointestinal tract from a surgeon's viewpoint is cited by T. A. Shallow (*Ibid.* 14:57 (Feb.) 1934). Teamwork is necessary for successful management. No definite rules can be laid down for all cases. Each case must be treated according to its individual requirements. For the successful removal of a foreign body which has passed the esophagus, the aid of the roentgenologist is always necessary. The esophagoscopist's part is played when the foreign body is lodged in the esophagus or is retained in the stomach. If the patient is seen before the foreign body has passed the pylorus, there will be no need for a surgeon. The endoscopic procedure has no mortality. Surgical removal is indicated in cases of persistently lodged foreign body. It is difficult for a foreign body to pass through the duodenum, but when it does so, it will usually pass entirely through the gastrointestinal tract.

The *indications for open surgical intervention* are

1. A persistently lodged foreign body which is shown to be in the same position on repeated x-ray examinations.
2. A foreign body which causes persistent abdominal pain.
3. A foreign body lodged at any point in the intestinal tract which causes pain, tenderness, and rigidity, indicating that it has penetrated the intestinal wall and is producing a local peritonitis.

Immediately before the patient is placed on the operating table, an x-ray picture should be made to determine the location of the foreign body and to compare its location as shown by the previous x-ray examination

If the foreign body has moved and there are no indications of peritonitis, operation should not be undertaken and the patient should be returned to bed.

When the foreign body is found in the first or second portion of the duodenum, it can readily be returned by manipulation into the stomach, where its removal may be accomplished without difficulty and without the risk of producing a narrowing of the duodenum. When it is located in the third portion of the duodenum, this procedure should be attempted but is not accomplished so easily.

The removal of foreign bodies from the intestinal tract below the duodenum is not difficult, but the author questions whether it is necessary unless there is evidence of perforation, indicated by peritonitis

Surgical intervention should not be recommended unless repeated x-ray examination or evidence of perforation shows that the foreign body will not pass

Having traversed the duodenojejunal junction, the foreign body will usually pass out of the body without interference.

In cases of persistently lodged foreign bodies and those with evidence of peritonitis or constant pain, surgical intervention is necessary.

**INTESTINAL OBSTRUCTION.—*Etiology.*—*Congenital Anomalies.*—**A case of *complete atresia of the terminal ileum associated with malrotation of the colon* in an infant 2 days old, is reported by T. F. Corkill and H. K. Corkill (Australian and New Zealand J Surg 3:352 (Apr) 1934). This case differs from others reported in both the type of the obstruction and the operative procedure

There was complete absence of the distal half of the ileum, the intestine being continued as an attenuated cord without an apparent lumen. In the middle of the attenuated cord there was a blind intestinal loop which appeared normal in every respect. There was no mesenteric defect. The ascending colon disappeared behind the mesentery of the small intestine, and no transverse colon could be identified.

The operation consisted of **side-to-side anastomosis** between the dilated ileum and collapsed sigmoid plus an **enterostomy** about 15 cm above the point of obstruction.

The enterostomy functioned well until the fourth day, when a normal bowel movement occurred by rectum. The catheter came out at that time and was not replaced. The bowel movements increased with a corresponding decrease in drainage from the enterostomy. The enterostomy closed during the fourth post-operative week. In the 5½ months which have elapsed since the operation, the infant has remained well and has developed normally.

The authors admit that the addition of the enterostomy in their case was probably unnecessary, but state that at the time of the operation they were not acquainted with the knowledge that such a procedure, whether alone or in combination with anastomosis, had hitherto been uniformly fatal in such cases.



It is the belief of C. W. Roberts (South. Surgeon 2. 301 (Dec.) 1933) that *stasis* in the intestine subjects the organism to the same potential dangers that attend obstructive lesions in other excretory systems of the body. Though wide variations in habit are commonly seen, there must necessarily be a physiologic normal in which minimal intoxication occurs. Good function rests on a structural pattern that guarantees adequate muscle tone, ordered permeability and uninterrupted gradients of peristaltic motion. The anatomic deficit regularly associated with the intestinal invalid is not susceptible to appreciable alteration by operative attack. These patients belong to the sphere of the internist and the psychiatrist. In a large proportion, however, much depends on the surgeon's interest in the developmental anomalies of the intestine, and the symptoms will be found due wholly or in part to mechanical factors susceptible to correction by the application of only sound surgical principles. When the toxic intestinal tide flows uninterruptedly until the compensation of vital organs, such as the liver, is lost, there arises a vicious chain that will not yield to attack on the focus in the intestine alone.

**CHRONIC DUODENAL ILEUS.**—The history of this condition is reviewed by E. Kraas and W. C. Beck (Ann Surg 99 311 (Feb.) 1934). The authors believe that the duodenum may assume a dilated state as the result of various factors acting either separately or in combination. American and English surgeons are inclined to ascribe dilatation of the duodenum to demonstrable mechanical causes, but many European surgeons have reported cases of a condition they call "true megaduodenum" in which no such causes could be found. For an understanding of true megaduodenum, it is necessary to know the embryological development of the duodenum, which the authors review in detail.

The various types of duodenal ileus are classified by the authors as follows:

1 *Idynamic duodenal ileus*—Of this type are cases in which no mechanical obstruction can be found, *viz.* the true megaduodenum of Duval, Melchior, Schmieden, and Kraas. The etiology still remains to be cleared up definitely. The condition has been attributed to developmental and neuromuscular factors and by some has been classed with Hirschsprung's disease.

2 *The dynamic chronic duodenal ileus*—Of this type are cases in which mechanical hindrance in the duodenum is discernible. On the basis of the nature of the obstruction, the following sub-groups are to be distinguished:

(a) *Intrinsic duodenal lesions*—Of this type are diseases affecting the duodenum itself, such as neoplasms, duodenitis, congenital atresia, inflammatory disease, a duodenojejunal kink, and diverticula.

(b) *Extrinsic lesions*—To these belong the chronic arteriomesenteric occlusion, peritoneal strands and adhesions, and diseases of the surrounding organs which produce stenosis by pressure.

(c) Complications of duodenum mobile such as *hernia* and *intussusception*.

The *site* at which the stricture is produced in the cases of Group 2 is of greater importance from the standpoint of diagnosis and therapy than in obstruction of the small intestine. In most cases, however, this is determined by the anatomical relations of the etiological factor.

Chronic duodenal ileus has received more attention in the American and English literature than in the European. In clinics other than those reporting large series of cases, the diagnosis is made extremely rarely, probably because the condition is often not looked for. The clinical history and physical examination, although suggestive when the possibility of the condition is borne in mind, are far from being clear. The roentgenologist is often interested only in the duodenal bulb and overlooks pathological processes in the remainder of the duodenum.

Shattuck and Imboden found chronic duodenal dilatation to occur 4 times more frequently in females than in males. This may be explained by the relaxation of the abdominal muscles following pregnancy. It may be due in part also to the greater frequency of gall-bladder disease in the female, although Bryant found adhesions more common in the male. The subjects are usually of middle age and of the asthenic type.

**Pathology.**—R. L. Holt (Brit J. Surg. 21: 582 (Apr.) 1934) divides acute intestinal strangulation into those in which the venous circulation alone is obstructed and those in which both the arterial circulation and the venous circulation are blocked. A further subdivision into long-loop, intermediate, and short-loop strangulation is necessary, as Foster and Hausler have demonstrated the great dissimilarity in the resulting phenomena.

In the investigations reported it was found that in strangulation of a long loop (over 40 cm in the dog), the loop becomes engorged with blood plasma and cells. As much as 50 per cent of the circulating blood may be withdrawn into the area, which is incompatible with life. This bears out Blalock's work on experimental shock.

In strangulation of loops of shorter length, the loss of blood was insufficient to cause death. Bacteria soon invaded the strangulated loop and a large amount of exudate was poured from the segment. At first, the exudate was very similar to blood plasma and nontoxic, but after about 20 hours it became dark and fetid, and on intraperitoneal injection into an animal caused death. By replacing the loop contents with water and air, the author demonstrated that the origin of the toxic substance was the wall of the gut rather than the intestinal contents. He found that the toxin is heat-stable and that its virulence is not increased by boiling, also that it does not pass through a Berkefeld filter. It appears to be a proteose, not an exotoxin.

Pressure within the strangulated loop is at first maintained by tonic contractions of the intestinal musculature. After the musculature has lost its tone, it is maintained by the formation of gas. This pressure probably prolongs the period of exudation long after thrombosis of the vessels has occurred. In very short loops the amount of toxin escaping is not sufficient to cause death. The disintegration of the intestinal wall continues until perforation occurs. Death then results from either the obstruction or general peritonitis. In very small strangulations, such as those seen clinically in a Richter hernia, death is probably caused by the dehydration and alkalosis accompanying the obstruction.

R. R. Best, L. A. Newton and R. Meidinger (Arch Surg 27: 1081 (Dec) 1933) point out that it is now the opinion of most authorities that intestinal

obstruction may be classified either as simple obstruction or as obstruction with gangrene or interference with the blood supply. There is a gross difference between the two conditions. The presence of a toxic element in the second type is indisputable. The evidence indicates that in simple obstruction a definite toxin is not the cause of death.

In early reports great emphasis was placed on the presence of a newly-formed and exceedingly toxic substance in the fluid contents above the obstruction and an increase of absorption resulting from increased pressure and changes in the mucous membrane. Since these reports, a great many investigators have attempted to prove that death is caused by a toxin absorbed above the level of the obstruction in combination with a disturbance of the acid-base equilibrium.

Wangensteen demonstrated by careful experiments that the contents of the normal and the obstructed intestine are equally toxic, and that the contents below the obstruction are apparently even more toxic than those above it. The rate of absorption and the selectivity from above or below the obstruction were not considered in these experiments.

It seems logical to the authors that if no specific toxin is present in obstructed loops free from gangrene, the lethal factor must be either increased absorption of substances normally present in the intestine or the failure of a neutralization process or buffer reaction which would ordinarily occur when the contents of the upper and lower intestines mingle. It is possible also that this failure may affect the function of the secretion of the intestinal mucosa and in some manner play a rôle in the causation of death.

Since considerable evidence has been presented to disprove the presence of a specific toxin in the obstructed intestine, the authors concluded that if absorption above the obstruction could be shown to be decreased or at least not increased, there would be some evidence that the cause of death is the failure of a neutralization process or buffer reaction to take place as it would normally when the different levels of intestinal contents mingle.

The authors were unable to demonstrate any increase in the rate or selectivity of absorption above or below the level of obstruction. If Wangenstein's finding, that normal intestinal contents are as toxic as the contents above and below an obstruction, is accepted, it may be assumed that there is no specific toxin which develops after the onset of obstruction. Wangenstein's experiments suggest that there is no increase in the rate or selectivity of absorption above the obstruction, and this seems strong evidence that the increased absorption above the obstruction cannot be the cause of death. Wangenstein's experiments tend also to rule out the probability of increased absorption below the obstruction.

The authors, therefore, believe it to be within the realm of probability that death following intestinal obstruction is due to a failure of neutralization or buffer reaction to take place between upper and lower intestinal contents in the lower part of the intestine. This need not be interpreted in terms of the development of a definite toxin, it is rather a physiochemical reaction that usually takes place when the contents of the upper and lower parts of the intestine are permitted to intermix. With this phenomenon there occurs absorption or failure of absorption of a substance, X, which causes a disturbance not in accord with nor-

mal cellular function and incompatible with life. The best clinical evidence in support of this theory is the fact that an obstruction of the distal colon is compatible with life for some time. This may be explained by the fact that the intermixture of upper and lower intestinal contents has already occurred above the obstruction and absorption has taken place. If the obstruction occurs above the distal colon, in the more active secreting levels and the absorption area, death occurs earlier than when the obstruction occurs lower.

M. A. McIver (Am. J. Surg. 22:579 (Dec.) 1933) shows that the absorption of the toxin in acute intestinal obstruction never occurs from the normal mucosa as is evident from the fact that the injection of highly toxic material into the lumen of the intestine of normal animals produces no symptoms. However, following changes in the mucosa, due usually to interference with the blood supply to the gut, the toxic material is absorbed. The absorption may be brought about by increased intrainestinal pressure or interference with the blood supply. The route by which the toxins are absorbed from the lumen of the bowel has not been proved. Three possibilities are: (1) the blood stream, (2) the lymphatics, and (3) the general peritoneal cavity.

Relatively recently the importance of dehydration and loss of chlorides in intestinal obstruction, especially obstruction high in the intestinal tract, has been emphasized. Stagnation of blood in the splanchnic area and anemia of the vital centers is thought by many to be the cause of symptoms and death. In considering death in intestinal obstruction it is important to differentiate between the levels at which the obstruction occurs. In high obstructions, death is due to loss of fluids and electrolytes. In simple low obstructions of the small intestine the marked distention of the bowel causes interference with the blood supply to the intestine which probably favors the development and absorption of toxins. In obstruction in the colon, death is probably brought about in the same way. In cases of strangulation it is due to the production and absorption of toxins and possibly the development of peritonitis.

A study of the electrolytes in intestinal occlusion by F. Cataliotti (Polichinico sez. chir. 41:17 (Jan.) 1934) shows that the quantitative changes of calcium, magnesium and phosphorus occur independently of the seat of occlusion, whether the obstruction be in a high, middle, or low situation. The values of calcium and phosphorus tended to increase with the aggravation of the clinical picture. The magnesium increased immediately after operation and continued to increase indefinitely.

**Symptoms.**—In this disease entity Kraas and Beck (*loc. cit.*) state that the symptoms are not accurate or definite, and the diagnosis is often difficult even after careful x-ray examination. Kellogg suggests that in many cases symptoms appear only when the colon is dragged downward by its contents, being therefore characterized by a certain periodicity. Taylor observed that symptoms result when the obstruction is greater than can be overcome by peristaltic efficiency. By many, 2 types of subjective symptoms are differentiated, *i. e.*, the mechanical and the toxic. The *toxic symptoms* consist of mental lassitude, fatigue, and headache. The latter is usually of the unilateral migraine type. The *mechanical symptoms* classified by Wheelon as static and kinetic and the symptoms empha-

sized by others are discussed by the authors in detail. The chief characteristics of the symptoms are periodicity of the attacks, the fact that any food may bring them on, the occurrence of headache and lassitude, and the fact that relief is obtained by the assumption of a bizarre position rather than by medication.

**Diagnosis.**—The *physical findings* are minimal, according to Kraas and Beck (*loc cit*). The patient is often of the asthenic type with a lax abdominal wall and a ptotic habitus. The upper abdomen may be distended, and the umbilicus may appear to be higher than normal. According to Hayes, percussion will give a tympanic sound behind the right rectus muscle and just to the right of the pylorus. The pleximeter finger must be placed with sufficient pressure to diminish gastric and colonic tympany, so that the examining finger is brought closer to the duodenum. Pressure upward and backward beneath the transverse colon permits the duodenum to empty. Gas can then be heard, felt or heard rushing into the jejunum. Thereafter the sound will be relatively dull. Case has described succussion over the duodenum. Zade used a stomach tube and compared the amount of water introduced into the stomach with the amount he was able to recover.

**Prognosis.**—K. A. Meyer and J. L. Spivack (Illinois Ann. Surg. 100: 148 (July) 1934) have observed that the mortality of surgically treated cases of acute intestinal obstruction has been reduced but little in the past 25 years. In their series of 505 cases it was 48.6 per cent. The high mortality is due to late surgical intervention when the "triad" of symptoms is present. This "triad" appears late, when the patient is practically moribund. Injection of physiologic solution of sodium chloride and dextrose cannot compensate for the damage of delay and does not influence appreciably the degree of mortality. It will be reduced appreciably only by early operation and this will be possible only when early diagnoses are made by the use of flat x-ray pictures as a routine measure. A "herring-bone" appearance shows the earliest stage of obstruction, a "step-ladder" appearance shows a more developed process and "fluid levels" show the well-advanced intestinal obstruction. In every postoperative abdominal case in which intermittent abdominal pain arises, it is advisable to take an x-ray picture by a portable apparatus and not to wait until the grave "triad" appears.

**Treatment**—Conservative treatment is directed against the ptosis and has an effect only in a palliative sense, according to Kraas and Beck (*loc cit*). Holmes recommends **long bed rest** and **over-alimentation** for cases of the *visceroptic type*. Others have recommended **rest in a moderate Trendelenburg position** and the wearing of **abdominal binders and supports**. **Massage of the abdominal wall** and **postural exercises** may prove beneficial. Very **frequent small feedings of food with a high calory content** and the administration of **mild laxatives** to prevent constipation are of value.

**Operative interference** should not be attempted before the patient's general health has been carefully determined. Wolfer states that in some cases the patient may remain in good condition in spite of high-grade obstruction. However, a sudden anatomical accident may cause an acute exacerbation characterized by severe toxemia. In the cases of patients who are extremely ill and can tolerate little surgical trauma, **repeated duodenal lavage** with the **Levine or Rehfuess**

**tube** is of distinct value. To combat the toxemia, the method of Dragstedt, *i. e.*, the **intravenous infusion** of 500 c.c. (1 pint) of **Ringer's solution** every 4 hours for 24 hours, may be employed. To overcome deficiency in the blood chlorides, Haden and Orr recommend the **infusion of sodium chloride solution**.

The choice of the operation is in many cases difficult and should be governed by the cause of the condition. Because of the great variety of etiological factors, numerous procedures have been recommended. The intrinsic lesions are usually treated by a **nutrient jejunostomy** or one of the **short-circuiting operations**. The various operations are described.

After operation, the **foot of the bed** should be **elevated**. In the immediate postoperative treatment the usual routine should be that followed after gastric surgery. Later, the patient should wear a **supporting belt** and should be given **exercises to strengthen the abdominal musculature**.

*Use of Drugs*—T. G. Orr (Ann. Surg. 98: 835 (Nov.) 1933) states that the beneficial results claimed for the **opium** and **morphine** treatment of peritonitis have been based upon false conceptions of the action of morphine on the intestines. The author insists that there must be some other basis than the abolishment of intestinal activity. In experiments on dogs, he has found that therapeutic doses of morphine sulphate definitely increase the bowel tone and the amplitude of the segmentation movements and initiate peristaltic waves. Large doses abolish the peristaltic action and somewhat decrease the tone, but do not affect the rhythmic contractions. Very large doses increase the amplitude of rhythmic segmentation movements. Clinical observations in cases in which ileostomy has been done and in cases of thin-walled herniæ also indicate that morphine definitely stimulates the activity of the small bowel. The constipating effect of morphine is apparently due chiefly to its spastic effect on the sphincters.

Clinical application of the findings of these experiments is possible in acute peritonitis and intestinal obstruction, in which overdistention of the small bowel is the most dreaded feature. As the distention increases, the circulation through the wall decreases and the bowel activity is correspondingly reduced. Thus, toxic material is absorbed, while gases are not absorbed. As **morphine** definitely stimulates the tone and rhythmic contractions of the bowel, its use is logical to prevent overdistention. The author believes there is no foundation for the supposition that such stimulated bowel activity spreads infection. In addition to its action on the bowel, morphine relieves pain and restlessness and thereby conserves the patient's strength. The maximal benefits can be obtained only by giving morphine in sufficient doses to produce continuous narcosis (every 4 hours). *Danger signals* are respirations below 12 per minute and cyanosis.

In the treatment of any intraabdominal condition associated with distention of the small bowel, special attention should be paid also to the maintenance of water, chemical, and metabolic balance. This calls for the administration of **sodium chloride** and **water**. As an aid, especially in the prognosis, frequent auscultation of the abdomen should be done during morphine treatment of abdominal distention. The presence of gas and liquid in a distended bowel gives

a characteristic tinkling sound during bowel activity which is totally different from the more muffled sounds of the normally functioning gut.

**Hypertonic salt solutions** have been used by many clinicians in the treatment of ileus. A Ochsner, I M Gage and R. A. Cutting (Arch Surg 27:742 (Oct ) 1933) report an investigation which they carried out on dogs to determine the relative efficacy of various hypertonic solutions

It seems apparent from their findings that a hypertonic solution containing calcium and potassium in addition to sodium is more efficacious in stimulating intestinal activity than a hypertonic solution of sodium chloride alone. This conclusion is supported by the authors' clinical experience in the use of hypertonic solutions of sodium chloride alone and "hypertonic" Ringer's solution

A. L. Abel (Lancet 2 1247 (Dec 2) 1933) states that in 50 cases of normal convalescence from a laparotomy he used **acetylcholine** routinely in the *post-operative treatment*, starting with 0.1 Gm ( $1\frac{1}{2}$  grains) 36 hours after the operation and repeating this dose every 6 hours until flatus or feces were passed without an enema. This result is obtained in many entirely untreated cases in from 6 to 12 hours.

In numerous cases of general peritonitis in which he used **acetylcholine**, Abel gained the impression that the postoperative course was more favorable than it would have been without such treatment. However, he believes that acetylcholine must be used in many more cases before it can be recommended for the postoperative treatment of every case in which laparotomy is done

In several cases in which there was doubt as to whether the condition was due to mechanical or paralytic obstruction, Abel gave 0.1 Gm ( $1\frac{1}{2}$  grains) of acetylcholine hourly for 6 doses. By this treatment, operation was frequently avoided. In cases of organic obstruction no untoward effects were produced. Most patients with severe postoperative distention, gas pains, and paresis of the bowels are considerably benefited by the administration of acetylcholine by intramuscular injection. In paralytic ileus, acetylcholine appears to be almost specific in effecting a cure

*Continuous Suction*—The pyloric balance in ileus treated by continuous suction from the stomach has been studied by W. Bartlett, Jr (Am J Surg 23 484 (Mar ) 1934). The author urges continuous positive suction of the stomach as a curative measure and as an aid to the understanding of the deranged physiology of ileus and the course of recovery from the condition

With the author's suction apparatus, the gastrointestinal status may be ascertained with mathematical accuracy. It is possible to measure in cubic centimeters the fluid passing over the pylorus per unit of time and to ascertain its direction under the influence of the tonus of the stomach and intestines and of peristalsis or reverse peristalsis. If the patient is not permitted to have fluids by mouth, there are only two factors to be considered: how much fluid has run out of the can and how much fluid is in the basin. By subtracting the former from the latter, the amount of fluid withdrawn from the stomach and duodenum is determined

However, the author prefers to give fluid by mouth and this adds a third factor. To determine the amount of fluid withdrawn in excess of the amount of

fluid drunk, or the amount of fluid retained by the patient, the fluid drunk is subtracted from the result obtained by the calculations described in the preceding paragraph.

If the result of the last subtraction is a positive number, if the contents of the basin are greater than the amount flowing from the can and the amount drunk by the patient, the remainder has been recovered from the stomach and there is a negative pyloric balance. If, on the other hand, the amount of fluid in the basin is less than the sum of the fluid drained from the can and drunk, there is a positive pyloric balance, as this indicates resumption of movement of fluid in the normal direction and progressive improvement.

The author has yet to see any harmful result from leaving a nasal catheter in position. The longest period over which he has used one continuously was 9 days. The catheter is lubricated with white, sterile vaseline before its passage, and oil of rose with a 0.5 per cent content of phenol is dropped into both nares every 6 hours. As a rule, the catheter is withdrawn, cleaned, sterilized, and inserted through the opposite naris every 24 hours.

In analyzing the charts, the negative or positive pyloric balance per hour is determined. This is done by dividing the pyloric balance by the number of hours over which the calculations were made. When a positive pyloric balance of from 90 to 100 c.c. per hour on continuous suction is attained and represents well over 50 per cent of the total intake by mouth per hour, the nasal catheter is clamped off to interrupt the syphonage as well as the positive suction. The patient is then given from 180 to 200 c.c. of fluid to drink within a half-hour. Two hours later the stomach is emptied by suction with a syringe. This procedure is repeated over a period of from 8 to 10 hours, and if not more than about 30 c.c. is recovered each time, the nasal catheter is removed and not more than 90 c.c. of water per hour is given by mouth for the next 24 hours. Gradually, the fluid intake is increased.

Increasing experience with this type of treatment indicates that there is a large group of cases of intestinal obstruction in which the danger of death is less if decompression of the bowel is brought about by continuous suction of the stomach than if operation is performed more than a very few hours after the onset. Cases of strangulated obstruction are obviously not included in this group.

**INTUSSUSCEPTION.—Etiology.**—According to W. Obadalek (Beitr. z. klin. Chir. 159-160 (Feb. 15) 1934), sudden increase in the intraabdominal pressure is, in many instances, the determining factor in intussusception of children. He reports a case in a girl who suffered from colicky pains about the navel for some time and in whom severe symptoms of invagination followed immediately a fit of severe paroxysmal cough. In a second case, symptoms of invagination followed straining at stool. At operation in this case there were found polypi in the small intestine. In both cases local spasms were present but appeared in themselves insufficient to cause intussusception. This was precipitated by a sudden increase in the intraabdominal pressure. A local spasm of the intestine causes pain, which provokes in a child a fit of crying, which in its turn increases the intraabdominal pressure. The latter may be of accidental nature, resulting from straining at stool, coughing or trauma. The author explains his



failure to produce experimental invagination in animals by the absence in them of the factor of considerable intraabdominal pressure. The peculiar predilection to invagination, so far as the age, the sex, and the state of muscular development are concerned, is best explained by the part played by the intraabdominal pressure

H. Koster (Am. J. Surg. 22:465 (Dec ) 1933) reports 5 cases of intussusception due to a *benign tumor*. Four of the patients were children. It is estimated that polypi are present in 5 per cent. of cases of intussusception. From the review of the literature, the impression is gained that intussusception is primarily a condition of infancy, which occurs most frequently in well-nourished, usually breast-fed infants. Its onset is often preceded by diarrhea or an error in diet. Castor oil may be an important factor in its production by causing violent and irregular peristaltic contractions.

H. N. Harkins (Ann. Surg. 98:1070 (Dec ) 1933) reports 2 cases of intussusception due to an invaginated *Meckel's diverticulum*, occurring in children. The author reviewed 160 cases which he collected from the literature. Harkins states that, as compared with the ordinary type of intussusception, this type occurs in older persons, is preceded more frequently by previous attacks, runs a more chronic course which is often characterized by a mild attack 1 or 2 days prior to the onset of the major illness, causes more severe vomiting, is associated with a palpable mass situated more often on the right side than on the left side, and much less frequently with a mass palpable through the rectum, and is accompanied by less profuse bleeding from the rectum.

**Symptoms.**—The symptoms of intussusception, as pointed out by Koster (*loc. cit.*), are, with few exceptions, similar to those resulting from intestinal obstruction. All are referable to the sudden occlusion of the lumen of the intestinal tract. Most prominent is abdominal pain, colicky in character, accompanied by paleness, drawing up of the legs, screams, and usually vomiting. Vickers found this typical onset in 87.5 per cent. of cases. Instead of the ordinary bowel movement, there is very frequently the passage of blood and mucus. This is almost pathognomonic.

In most cases an abdominal tumor can be felt. The tumor is sausage-shaped, about 1 inch in diameter, of variable length, and hard. It becomes more definite during the spasm of pain and may almost disappear during the interval of freedom from pain. It may be detected anywhere in the colon, but is found most frequently in the left side of the abdomen. It is tender, and its manipulation produces spasm. The blood which appears from the anus is usually bright red and intimately mixed with mucus, which gives it a red-currant-jelly appearance.

**Differential Diagnosis.**—Intussusception must be differentiated from *acute enterocolitis*. Both conditions are frequently preceded by digestive disturbances such as diarrhea, vomiting, and the passage of blood and mucus from the rectum accompanied by tenesmus. The crucial point in the diagnosis, according to Koster (*loc. cit.*), is the demonstration of complete intestinal obstruction. Such obstruction is evidenced by mucus on the diaper and bile in the blood. In acute intussusception the onset is usually very sudden.

Intussusception must be differentiated also from *Henoch's purpura*. The latter usually occurs in older children and is never accompanied by true intestinal obstruction, fecal matter always being found mixed with the blood and mucus passed by rectum. Moreover, in purpura, rectal examination discloses a characteristic edema of the mucosa and if an iliac tumor is present, it is fixed, usually situated in the left iliac fossa, and due to infiltration of the colon by hemorrhage. During the course of purpura, ecchymotic spots make their appearance around the joints of the extremities.

When an intussusception protrudes from the anus, it may be mistaken for *prolapse of the rectum*. The differentiation is made by the examining finger which in true prolapse cannot be inserted between the protrusion and the walls of the rectum, whereas in an intussusception it can be swept completely around the prolapse.

**Prognosis.**—Koster (*loc cit*) states that this depends in large measure on the duration of the condition before treatment is begun. The type of the intussusception is also a factor. Ileocolic intussusception is the type most difficult to reduce and the first to show gangrenous changes. Enteric intussusception comes next in these respects. Spontaneous cure does not occur in more than 1 or 2 per cent of cases.

**Treatment.**—The treatment is **surgical**. The air and water reduction methods are dangerous, according to Koster (*loc cit*), because of the early circulatory changes in the affected bowel which diminish the resistance of the bowel to pressure and favor perforation. However, Hipsley recently recorded 100 consecutive cases treated by **hydrostatic pressure** with a mortality of 5 per cent and complete reduction in 62 per cent.

The *operative procedures* indicated vary according to the nature of the condition. Tension on the intussusception is usually ineffective and not without danger. The safest and most satisfactory procedure is backward pressure on the apex of the intussusception by successively enclosing more and more of the intussusciens in the hands in a retrograde direction. When reduction is difficult, the previous maneuver may be augmented by pulling upon the entering loop. If this is not sufficient, it is advisable to wrap the entire tumor in a warm wet pad and then, applying pressure equally in all directions, squeeze the mass with the hands. This reduces the bulk by displacing some of the liquid from the wall into the lumen and facilitates reduction by the measures which previously were unsuccessful.

The apex of the intussusception should then be carefully examined for tumor. Because of the edema, it is often difficult to determine the presence of a neoplasm. Under such circumstances there should be no hesitancy in incising the intestine in a longitudinal direction to accurately ascertain the condition. If a **tumor** is discovered, it should be removed by local **excision** or **enterectomy**, unless the patient's condition will permit no further operative treatment. Malignancy is encountered more frequently in the large bowel than in the small intestine and more frequently in the adult than in the child. Pedunculated tumors are far less likely to be malignant than tumors without a pedicle. When a *sessile tumor* is

definitely *benign*, its complete destruction may be accomplished with the **cautery** without enterectomy.

In all resections in children, the continuity of the intestinal canal will be most easily and safely restored by lateral anastomosis after end-closure.

In the choice of **anesthesia**, **subarachnoid block** should be considered first. It produces no shock, prevents operative trauma, facilitates reduction of the intussusception, causes no tissue irritation, combats ileus, does not abolish the cough reflex, and is easy to induce and safe.

*Postoperatively*, a 5 per cent **solution of sodium chloride** should be given intravenously. **Fluids** should be **forced**. A 20 per cent. **solution of glucose** should be given intravenously if vomiting prevents its oral administration, and **insulin** should be given subcutaneously. **Hypodermoclysis** is often a very valuable aid. When reduction is impossible or gangrene has developed, the condition of the patient determines the choice of treatment. The procedures to be considered under such circumstances are (1) **resection with intestinal anastomosis**; (2) **resection with enterostomy**; and (3) **wrapping of the intussusception in omentum** followed by **enterostomy with resection and anastomosis** after the urgent symptoms of obstruction have subsided.

**JEJUNAL ULCER.**—It is pointed out by D. P. D. Wilkie (*Ann Surg* 99:401 (Mar.) 1934) that *postoperative* jejunal ulcer occurs much more frequently in patients who, before operation, have a high gastric acidity and little gastric retention. It is observed but rarely in patients with pyloric or duodenal stenosis of long duration and low gastric acidity. It was in the treatment of the latter type of case that the reputation of the operation of gastrojejunostomy was founded, and if the operation had been restricted to that type, jejunal ulcer would not be the problem that it is today.

**Treatment.**—Cases of *duodenal ulcer with high acidity* and little or no stenosis should be treated by **gastroduodenostomy** or some other form of **plastic operation** at the pylorus. Injudicious or heavy handling of tissues and the use of clamps at operation may lower the tissue vitality and thereby lead to the formation of a stomal ulcer in the early postoperative period. The operation should be regarded, not as a cure, but rather as an incident in the treatment of peptic ulcer. Regulation of the **diet** and the use of **alkalies** during the early months of convalescence are imperative. The sensitive duodenum should be protected from hyperacid gastric juice until it has acquired immunity. Neglect of these reasonable precautions must inevitably lead to a high incidence of jejunal ulcer.

The most common *complications* of jejunal ulcer are

1. *Recurrent hemorrhage*. This is very frequent and most difficult to treat. It requires **surgical intervention** preceded by **blood transfusion**.

2. *Perforation* into the free peritoneal cavity. While uncommon, this requires **closure** without compromising the gastrojejunal outlet. If the patient survives this intervention, a second **operation** directed at the ulcer and presenting a formidable technical problem is necessary.

3. *Subacute perforation* with the formation of an inflammatory mass. This calls for **conservative treatment** until the inflammatory reaction has subsided.

Later a **partial gastroduodenostomy** should be performed. When the general condition is poor and the inflammatory infiltration of the mesocolon and the root of the mesentery is such as to make a resection formidable, reasonably good results are obtained by a double short-circuiting operation, *i. e.*, **gastroduodenostomy** to exclude the old ulcer and **duodenojejunostomy** to exclude the region of the jejunal ulcer. In cases of *jejunal ulcer penetrating into the mesocolon and posterior abdominal wall*, excision of the ulcer should not be attempted, as it may damage the superior mesenteric vein. In such a case in which the ulcer was in the proximal loop, satisfactory results were obtained by **removing the gastroenterostomy stoma**, closing the stomach and jejunum, establishing a **gastroduodenostomy** opening to exclude a stenosing duodenal ulcer, and performing a **duodenojejunostomy** to short-circuit the jejunal ulcer. Many of these *jejunal ulcers* are *complicated by duodenal stasis* secondary to thickening and fibrosis in the region of the stoma which leads to gradual narrowing and in some cases potential, if not actual, occlusion of the gastroenterostomy opening. Cases with such lesions must be treated by **drainage** of the partially obstructed duodenum before complete relief can be afforded. In some cases, drainage of the duodenum by the establishment of a **duodenojejunostomy** may be sufficient. In others, this operation must be associated with a direct attack on the jejunal ulcer and the original stoma. The author reports 2 illustrative cases.

*Jejunocolic* or *gastrojejunocolic fistula* is always serious. The mortality of a 1-stage radical operation is very high, almost 40 per cent. As the patients are usually in poor condition a **2-stage operation** is advisable. The author reports a case in detail. The patient had a fistula between the posterior wall of the stomach and the splenic flexure of the colon. As it was deemed inadvisable to detach the colon from the stomach where both were fixed, infected, and edematous, the portion of the colon involved in the fistula was excluded by isolating the loop of colon attached to the stomach and the continuity of the colon was restored by an end-to-end anastomosis. Later, when the patient was in better condition, the isolated colon loop was excised with the gastric ulcer and a part of the gastric wall around it. The patient made a rapid recovery and remained in good health.

The *perforation of postoperative peptic ulcer of the jejunum* into the free peritoneal cavity has been studied by M. Makkas (Beitr. z. klin. Chir. 159: 61, 1934), basing his article on 131 cases collected from the literature. The author chose only cases which were reported in detail. He states that the incidence of such ulcers is doubtless very much higher than is suggested by this number, as at least 170 cases have been reported. In general, however, jejunal ulcers perforate less frequently than gastric and duodenal ulcers.

Perforation into the free peritoneal cavity occurs more often after anterior than after posterior gastroenterostomy. This is easily explained by the anatomical relationships. As a rule, jejunal ulcers perforate less often than gastrojejunal ulcers. In the literature attention is frequently called to the fact that a perforating jejunal ulcer is often preceded by a perforating duodenal or gastric ulcer. Patients treated for perforation of a jejunal ulcer by simple closure of the perforation very often have another, or more than one, perforation at the same site.

or develop a new jejunal ulcer. In 16 of the cases reviewed by the author, there were 45 ulcer perforations. In contrast to jejunal ulcers, gastric and duodenal ulcers very rarely perforate a second time. The explanation for the unusual behavior of jejunal ulcers is not known. In many of the cases reviewed an anterior gastroenterostomy was performed primarily.

In the *treatment* of jejunal ulcer perforating into the free peritoneal cavity **simple suture with or without excision** is to be considered. In cases so treated the mortality ranges from 22 to 23.5 per cent and there is danger of subsequent perforation. In 7 of the cases reviewed **degastrostomy** was done. From his own cases and those reported in the literature, the author concludes that the **radical method** may be chosen when the patient's general condition will permit it and the topical relationships will not render the operation too difficult. In 24 cases treated radically the mortality was 8.3 per cent.

**TUBERCULOSIS OF INTESTINES.**—M. M. Brea (Semana méd 41:553, 1934) reports 8 cases of ileocecal tuberculosis from the clinic of Arce. While they were of different pathological types, they may be divided into 2 groups, according to the first complaints. In the *first group* were 4 cases in which pulmonary lesions were present, but because of the occurrence of acute pain in the right lower quadrant of the abdomen without a previous history of gastrointestinal trouble, operation was performed for appendicitis. In 2 of these cases there was a persistent draining sinus which required further surgery and a fecal fistula developed. In the other two a fistula appeared immediately after the appendectomy.

The *second group* included the cases of 4 patients with no clinical evidence of pulmonary tuberculosis, who had complained for years of gastric disturbances which had been attributed to peptic ulcer, gastropptosis, or partial intestinal obstruction. X-ray examination established the diagnosis and revealed latent fibrous lesions of tuberculosis in the lungs.

All fistulae following appendectomy which are not due to a foreign body, especially fecal fistulae, in individuals with a history or x-ray evidence of tuberculosis, should suggest the possibility of ileocecal tuberculosis.

The patient with chronic dyspepsia without a demonstrable peptic ulcer, but with pulmonary lesions demonstrable by x-rays, should be subjected to a complete x-ray study of the colon, especially the ileocecal region.

Surgical tuberculous lesions of the ileocecal coil are well localized at first and develop very slowly. The surgical treatment of choice of such lesions is **resection**, but **simple ileocolostomy with exclusion of the diseased segment** has resulted in cure in cases in which it was thought unwise to attempt radical removal. **Simple laparotomy** does not aggravate the course of the disease and at times seems to bring about improvement. It should, therefore, be performed as a diagnostic exploration in doubtful cases.

The anatomicopathological type of intestinal lesion coincides usually with the lesion found in the lungs. Its slow evolution is explained by its predominantly fibrous character. The condition of the lungs does not contraindicate operation. A more dependable criterion of the advisability of surgical treatment is the general condition.

**TUMORS OF SMALL INTESTINE.**—According to E. Lauwers (J. de chir 42 833 (Dec ) 1933), of the cancers of the small intestine those of the duodenum are the most common. They usually occupy the ampulla of Vater and may arise from the ampulla itself, the duodenal mucosa, the duct of Wirsung, or the head of the pancreas.

**Symptoms.**—Depending upon the origin of the tumor, the first result of cancer of the ampulla is obstruction to the flow of bile or the pancreatic secretion. Practically, however, the initial symptom is always icterus. The icterus may be slight and intermittent but usually is continuous and becomes progressively more intense. When there is complete obstruction the feces are clay-colored and heavily charged with fat and proteins and the urine is highly pigmented. When there is a complicating biliary infection, epigastric pain and fever occur. Eventually, hepatic degeneration and toxic nephritis develop and the patient dies with oliguria, vomiting, and deepening coma.

**Diagnosis.**—Physical examination reveals no tumor. The liver is large and, unless cholelithiasis complicates the picture, the gall-bladder is dilated.

Cholecystography shows only the absence of a gall-bladder shadow. X-ray examination of the gastrointestinal tract may reveal hyperperistalsis in the duodenum and occasionally a small defect in the inner border of the shadow of the second portion.

Analysis of the duodenal contents and of the feces for blood is usually negative

In the *differential diagnosis*, stone in the common duct, chronic pancreatitis, and carcinoma of the pancreas must be ruled out. In cases of stone in the common duct, pain precedes the icterus and the icterus is intermittent. In chronic pancreatitis and carcinoma of the pancreas there is no palpable tumor.

**Treatment.**—In cancer of the ampulla the treatment may be palliative or radical. Palliative operation consists of internal or external **drainage**. The results of both types of drainage are poor. According to Gosset, the mortality of internal drainage is 75 per cent and that of external drainage, 70 per cent. The radical operation consists of **removal of the tumor**. This was first performed by Halstead, in 1898. The patient died 7 months later from recurrence. In 1900, Mayo reported the case of a patient who survived the operation two years. At the present time about 64 cases are on record. In 57, the operation was done in one stage. In 51, the tumor was removed by the transduodenal route, in 2, by the retroduodenal route, and in 2, through the common duct. In 2 instances a segment of the duodenum was resected. Among the 7 two-stage operations, **cholecystostomy** was performed twice, **drainage of the common duct** twice, **cholecystoenterostomy** 3 times, **excision of the tumor by duodenotomy** 5 times, and **excision of the tumor by resection** of a segment of the duodenum twice.

The value of the radical operation depends upon the variety of the tumor. Tumors originating in the terminal portion of the common duct, in the duct of Wirsung, or in the duodenal mucosa, possess the degree of malignancy common to cancers of the intestine and metastasize to the regional lymph nodes. True tumors of the ampulla remain strictly localized for long periods.

The difficulties of a **radical operation** are much less formidable than is generally supposed. Whether the operation is performed in 1 or 2 stages, the *first step* should be diversion of the flow of bile. External drainage is to be condemned. For internal drainage a choice may be made between **cholecystogastrostomy**, **cholecystoenterostomy** and **choleodochoenterostomy**. Cholecystogastrostomy is undesirable because the gastric juice eventually damages the gall-bladder mucosa. Most surgeons anastomose the common duct to the duodenum. When this is done by Coffey's method there is no reflux of the duodenal contents. When the gall-bladder is dilated, an anastomosis with the jejunum is preferable. A long loop of jejunum or the Y-anastomosis of Montprofit should be used. The latter eliminates the danger of angiocholitis.

Depending upon the patient's general condition, the *second stage* of the operation, removal of the tumor, may be performed immediately or delayed for 2 weeks. The initial exploration to establish the presence of the tumor must be direct, through an incision of the duodenum. The tumor is often no larger than a pea and may be overlooked if only palpation of the duodenum is done. As the tumor is often friable or mobile, sounding of the common duct may also lead to error. The duodenum should be mobilized and then opened by an incision along the right border. The tumor has the appearance of a small cauliflower growth or an ulcer. When it is a cauliflower growth, it has arisen in the ampulla and is sharply outlined. When it suggests an ulcer, it is a malignant intestinal cancer and the surrounding mucosa is indurated. To excise the ampulla, a circular incision should be made. Usually this need be no deeper than the submucosa. If the muscularis is included, the pancreatic duct must be reimplanted in the duodenum and the common duct ligated at its origin.

Resection of the duodenum, with or without the head of the pancreas, is a difficult and shocking operation. Moreover, for cancer of the ampulla it is more extensive than necessary, and for cancer extending beyond the limits of the ampulla it falls short of a rational operation for malignancy. Coffey has systematized the technic but the procedure has been attempted only 5 times.

**Radium** therapy has apparently been employed only rarely. In one case, Abel (1924) fixed the radium in close contact with the tumor through a duodenal incision and for removal attached it to a heavy thread previously introduced by mouth. Handley (unpublished case) introduced needles into the neoplastic mass by the retroperitoneal route and brought the threads to which they were attached out of the abdomen through a large drain. Because of the marked edema produced by the radium and the menace of complete duodenal obstruction, a **preliminary gastroenterostomy** is essential.

The author gives the histories of 2 personal cases. Both patients were operated upon in one stage. **Internal drainage** of the bile was established by a **Y-cholecystojejunostomy**. A generous loop of the upper end of the jejunum was sectioned and the lower end passed through the transverse mesocolon and implanted in the gall-bladder. The upper end was anastomosed to the side of the lower segment of the loop, end-to-side. In both cases the tumor was small and could be excised by an incision of the mucosa and submucosa alone. When seen, respectively 9 and 46 months after the operation, the patients were in good health.

**LIVER.—INJURIES.**—D. E. Robertson and R. R. Graham (Ann. Surg. 98:899 (Nov) 1933) report 2 cases of subcapsular *rupture* of the liver with operation and recovery. In one case the seriousness of the injury was recognized early, the tumor appeared early and at operation the cavity was found to be filled only with blood. In the other case, there was a long latent period of well-being between the accident and the appearance of the tumor which at operation contained bile and blood and was accompanied by gross destruction of the tissue of the liver. If a patient suffers an abdominal injury with distress referred to the right side and accompanied by pain in the shoulder, early exploration is advisable, as there will be a shorter convalescence and it will avoid destruction of the tissue of the liver should the diagnosis prove to be a subcapsular rupture of the liver. If the tumor occurs soon after the injury, the authors presume that its contents will be blood, and **drainage with a tube** appears to be the ideal method of handling it. If it is late in forming, bile will constitute an important volume of the content of the cavity, and **marsupialization** is desirable.

**Diagnosis.**—In the x-ray diagnosis of rupture of the liver, W. F. Burke and J. P. Madigan (Radiology 21:580 (Dec) 1933) point out that thorium dioxide solution (thorotrast) is of practical use in the diagnosis of traumatism of the liver and spleen when the physical signs are obscured by any cause whatever. It apparently exercises no deleterious effects, even when administered to patients having overwhelming infections, and may be administered intravenously immediately on indication of an intraabdominal hemorrhage. Its use is not contraindicated in injuries involving the liver and spleen. One-half of the usual dose was sufficient to produce a shadow heavy enough for diagnosis, and an x-ray picture may be taken 4 hours after such an injection.

**In Newborn.**—According to G. Rogers (Am J Obst and Gynec 27:841 (June) 1934), the chief factor in the production of *hemorrhages* from the liver and *ruptures* of the hepatic parenchyma in the newborn is compression of the fetal liver. This type of trauma is not uncommon, often being produced by a doubling of the fetus in podalic version or by improperly directed traction during a breech extraction.

Early diagnosis is essential if the infant is to survive. To date, only one case in which surgical treatment was instituted in time to save life has been reported.

In the *diagnosis* the case history and the size of the infant are of special importance. Death occurs either immediately or on the third or fourth day of life. Immediate death may be due to a sudden large intraperitoneal hemorrhage. As a rule, such a hemorrhage is first diagnosed at autopsy. Death occurring 3 or 4 days after birth may be due to laceration of the capsule covering a subcapsular hematoma or the dislodgment of a clot formed previously in a parenchymal tear.

The condition is usually manifested by marked pallor, restlessness, a cry indicating pain, a subnormal temperature, perspiration, shallow and labored breathing, and abdominal distention with possibly, in advanced cases, a fluid wave.

The author emphasizes that in any case in which an intraperitoneal hemorrhage is suspected, abdominal paracentesis is a safe and reasonably accurate diagnostic procedure.



The first and most important step in the *treatment* is the **immediate transfusion of citrated blood**. The active **surgical treatment** indicated is exposure of the bleeding point and the establishment of hemostasis by suture and pack

**HEPATIC CHANGES FROM OBSTRUCTION OF COMMON DUCT.**—M M Lieber and H L Stewart (Arch. Path. 17. 362 (Mar ) 1934) describe the changes in the hepatic and bile ducts resulting from obstruction to the common bile duct by *carcinoma* of the head of the pancreas and submit evidence showing that cirrhosis may result from uncomplicated or noninfectious biliary stasis. The biliary conducting system undergoes a tremendous volumetric increase, with corresponding stretching and thinning of its walls. The process extends uniformly into the branches of the fourth and fifth orders. The vasa aberrantia and parietal sacculi become effaced. The canaliculi are distended with bile thrombi, many of which remain in place, although others are extruded into the tissue spaces and sinusoids, where they may be phagocytosed by Kupffer cells and macrophages. Bile pigment, in the form of granules or droplets and in colloidal suspension, may be found, chiefly in the cells of the central portions of the lobule.

Regressive lesions are present as mild and localized degenerative changes involving the hepatic cells about the central vein, as nonpigmented local nodular areas of necrosis, and as deeply pigmented biliary necroses occurring either in the outer portion of the lobule or within the portal radicle. The intrahepatic ducts elongate and become tortuous, and they show, in addition, a true proliferation. A new formation of connective tissue occurs simultaneously with the changes in the bile ducts until after the second month, when a rapid, independent and progressive proliferation takes place, resulting in a well-marked deposit of connective tissue, which is interlobular, intralobular and, in long-standing cases, even perilobular in distribution. The hepatic lobules show a corresponding reduction in size without much architectural alteration except at the peripheries, where atrophy may become well-marked. The walls of the branches of the hepatic artery undergo hypertrophy and those of the branches of the hepatic vein and, to a less extent, of the portal veins, show a new formation of fibrous tissue. The liver possesses little or no regenerative ability in the face of total stasis.

Experimental studies on the cause of death in *acute portal obstruction* produced by ligation of the portal vein were conducted by R. Elman and W. H. Cole (Arch. Surg. 28. 1166 (June) 1934). It seems clear to them that the rapid death which so regularly follows total occlusion of the portal vein is due to circulatory failure, because of extensive loss of blood from the general circulation into the trapped splanchnic area. No evidence of the production or absorption of a toxic substance (by guinea-pigs and white mice) was found. The evidence in favor of the purely physical factor was uniform and consistent. The increase in weight of the splanchnic area following occlusion of the portal vein was great enough, on the basis of the amount of entrapped blood it contained, to have caused death from shock alone. The fall in blood-pressure was similar to that noted after an extensive hemorrhage, except that the pressure was sustained at a low level until death. The behavior and appearance of the animal after ligation

of the portal vein were similar to those seen after marked loss of blood from hemorrhage.

Attempts to raise the blood-pressure and prolong life by transfusions of blood were successful, and it was possible to postpone death for more than 6 hours. It was possible to prolong life and prevent the characteristic fall of blood-pressure following occlusion of the portal vein by ligating the aorta above the celiac axis, which effectively stopped blood from entering the splanchnic area. These animals lived only a few hours, but they lived as long as animals with ligation of the aorta alone. The results of the experiment were the same if, in addition, several hundred cubic centimeters of blood were injected into the mesenteric arteries to produce the cyanosis and congestion ordinarily seen after ligation of the portal vein.

Death following ligation of the portal vein is probably hastened by the fact that ligation at the same time prevents the gastrointestinal tract from aiding in the loss of fluid. When a low blood-pressure is maintained too long, it can never be corrected, no matter how much blood is transfused. The effect may be due to changes produced in the nerve cells. It is likely that too low a pressure slows the metabolic exchange and causes irreparable alteration in the central nervous system. On the other hand, the defect caused by a low pressure may be due to increased capillary permeability.

**CIRRHOSIS OF LIVER.—Treatment.**—On the basis of a series of cases of cirrhosis of the liver reported in the literature and 1 case observed by the writers, in which **splenectomy** was strikingly beneficial, A. Bergeret, J. Caroli and R. Audeoud (Rev. de chir. Paris 53:111 (Feb.) 1934) attempted to determine the *indications* for splenectomy in this condition. They found that good results followed splenectomy in cirrhotoses of unknown cause occurring in young persons. In all of the cases the spleen was enlarged. The symptoms which particularly indicate surgical intervention are crises of hepatic pain, hemorrhage, anemia, jaundice, and pruritus. Even in the presence of marked ascites and profound impairment of the general condition, splenectomy has yielded excellent results.

Emile Holman (West J. Surg. 41:255 (May) 1933) proposes a new operation for hepatic cirrhosis, which consists of **implantation of the spleen in the abdominal wall**. The proposed procedure for the relief of *ascites* was suggested by certain observations made in the course of a splenectomy for Banti's disease which was characterized by a large spleen accompanied by considerable cirrhosis of the liver.

The outpouring of ascitic fluid was explained on the hypothetical probability that during life there had developed, due to the hepatic cirrhosis, a considerable collateral circulation by way of the spleen and its large vessels, the blood flowing in a reverse direction through the splenic vein from right to left. Removal of the spleen interrupted this collateral bed, and ascites occurred until adequate collateral circulation had again developed. This observation prompted the thought that a reversal of flow through the splenic vein might be an excellent procedure in the presence of ascites. Its feasibility was therefore tested out in animals.

*Experiment I.*—Through a midline incision the splenic artery was ligated, the spleen imbedded, after scarification of its surface, in the lateral abdominal wall, and a partial ligation of the portal vein was attempted. The dog died promptly within 36 hours and at necropsy there was generalized purplish discoloration of all abdominal viscera, due to complete ligation of the portal vein.

*Experiment II.*—On January 5, 1933, the splenic artery was ligated and the spleen, after scarification of its surface, was imbedded in the lateral abdominal wall. On February 7, 1933, the portal vein was partially ligated. The passage

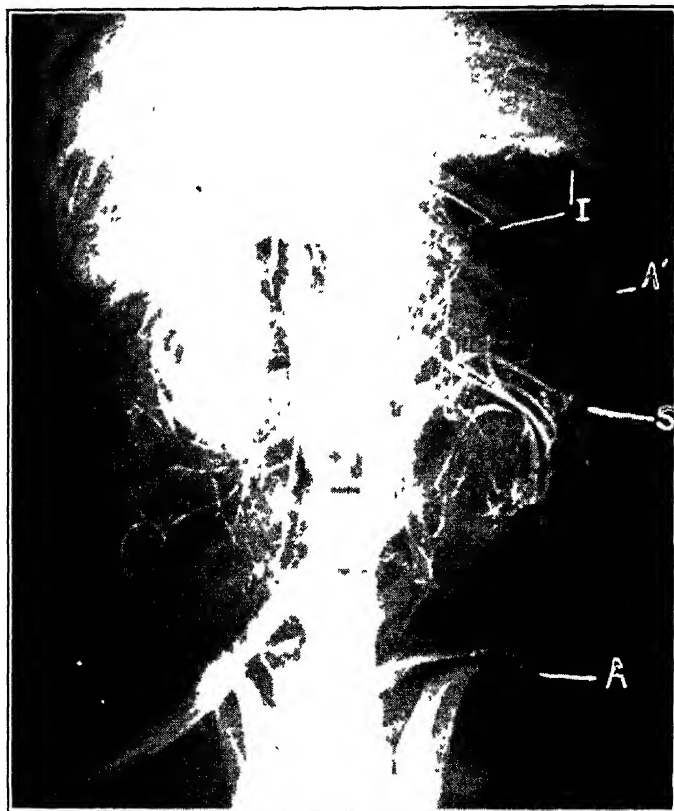


Fig 1—Visualization of portal tributaries following injection of inferior mesenteric vein. The spleen was implanted in the abdominal wall and the splenic artery ligated on January 5. On February 7 the portal vein was ligated. Animal was killed on February 18. The opaque material (bismuth oxychloride, 17 per cent in 10 per cent gum acacia) has largely escaped the portal system by a reversal of circulation through the splenic vein, thence entering the systemic circulation by way of the iliac vein and anastomotic channels *A* in the abdominal wall, as well as by way of the intercostal veins *I*, receiving blood from the veins *A'* in the lateral abdominal wall (E Holman West J Surg)

of several bloody stools in the next 24 hours indicated a probable congestion in the distribution of the portal vein. The animal recovered, however, and on February 17, 10 days after presumable partial ligation of the portal vein, exploration revealed seemingly complete closure of the portal vein. The dog was killed the next day. Necropsy showed no free abdominal fluid but almost complete closure of the portal vein, the ligature permitting passage of a small millimeter probe. Without displacing the organs, a cannula was inserted into the inferior mesenteric vein lying along the descending colon, and a suspension of bismuth oxychloride in a 10 per cent gelatin solution was introduced into the cannula.

Stereoscopic plates (Fig 1) revealed a moderate injection of the hepatic vessels through the small millimeter-sized opening in the portal vein and a remarkable collateral circulation running through the splenic vein into the lateral abdominal wall and thence into the intercostal veins and a large tributary to the iliac vein.

This experiment demonstrated conclusively that a reversal of flow could be produced in the splenic vein after ligation of the splenic artery, implantation of the spleen in the abdominal wall, followed subsequently by almost complete ligation of the portal vein. In the meantime, Holman was emboldened to attempt the procedure in man without any effect, however, upon the existing ascites.

The accumulation of ascitic fluid in hepatic cirrhosis is presumably due to portal obstruction. Definite evidences of such obstruction may be recognized on abdominal exploration by the enlarged and distended veins of the omentum, of the mesenteries and of the stomach and intestinal tract. In addition, they are tortuous and apparently increased in number. There may be and usually is enlargement of the spleen. Dilated and tortuous vessels will be found running from the cardia to the diaphragm and lower esophagus. Hemorrhoids are usually present. Such evidences of portal obstruction must of necessity be demonstrable before embarking on any procedure designed and calculated to correct this obstruction. The disappointing results obtained in the Talma-Morrison operation are not always an indictment of the operation, but a reflection on the surgeon's judgment.

The success of any operation for ascites is obviously dependent upon the correction of the cause of the ascites. In a careful analysis of 5000 cases of ascites by Richard Cabot, cardiac disease accounted for 1397 cases, renal disease for 665 cases, and only 325, or about 1 in 16, were found to be due to hepatic cirrhosis. Tuberculous peritonitis was responsible for 263 cases, pelvic tumors for 118, abdominal carcinoma for 109, and intestinal obstruction for 86.

The above unsuccessful example serves to illustrate the futility of operative interference in ascites due to some cause such as polyserositis unaccompanied by portal obstruction. Holman's only excuse for performing the operation was the remote possibility that even though obstruction was absent at that moment, its later development might be anticipated, and another route for the portal stream be provided. Incidentally, it served also to demonstrate the feasibility of the operation.

Summarizing, Holman states that, experimentally, practically the entire portal stream can be diverted through the splenic vein following ligation of the splenic artery and implantation of the spleen in the abdominal wall. Clinically, the procedure has been applied, demonstrating its feasibility, but without success, insofar as the ascites is concerned. Its success depends upon applying it in properly selected cases, and it is presented as a possible procedure in those instances of hepatic cirrhoses accompanied by unmistakable evidence of portal obstruction.

**MESENTERY.—ACUTE MESENTERIC LYMPHADENITIS.**—S L. Goldberg and I T. Nathanson (*Am J Surg* 25:35 (July) 1934) reviewed the cases of 16 children who presented a clinical picture very similar to that of acute appendicitis, but at laparotomy were found to be suffering from an acute

mesenteric lymphadenitis As all of the children had an infection of the upper respiratory tract, the authors suggest that the lymphadenitis may have spread by the hematogenous route from such a focus

**CHYLE CYSTS.**—The *symptoms* enumerated by A. N. Collins and G. L. Berdez (Arch. Surg. 28. 335 (Feb.) 1934) are malaise, loss of strength and weight, easy fatigability, nausea, occasional vomiting and abdominal discomfort varying from a dull ache to pain. In half of the cases a palpable tumor was found. Abdominal tenderness is nearly always present, being generalized in the majority of the cases. Rigidity occurred in the acute cases, usually suggesting intestinal obstruction or peritonitis. The tumor does not move with respiration. The presence of a freely movable tumor in the lower part of the abdomen which fluctuates and has a midline attachment should suggest mesenteric cyst. The *differential diagnosis* is aided by the discovery of chylous ascites on exploratory puncture.

Surgical *treatment* offers the only hope of cure. The mortality of all methods of treatment has been 25 per cent. The methods included (1) **aspiration**, (2) **incision and drainage**, (3) **enucleation**, and (4) **marsupialization**. The authors regard marsupialization as the best procedure.

In a careful search of the literature Walter E. Lee (Ann. Surg. 97. 465 (Mar.) 1933) found that 329 cases have been published to date. The origin of these cysts presents a difficult problem, but it seems probable that they are derived from aberrant remnants of the Wolffian body and that the embryonic disturbance occurs at various periods in the history of this structure.

Most of the reported cases have been in children, although the condition itself may be found at any age. The incidence in females is greater than in males, about 2 to 1. For the most part, mesenteric cysts are located in the vicinity of the terminal ileum and jejunum. Only about 10 per cent. of the reported cases have been located in the mesocolon.

There are no pathognomonic *symptoms* or signs which make for the *diagnosis* of mesenteric cysts. The symptoms are due, for the most part, to the size of the tumor and its encroachment upon the lumen of the intestine. If the growth is a rapid one, the symptoms are acute. Hence, acute intestinal obstruction, with all its signs and symptoms, develops. If of slow growth, there are symptoms and signs of a chronic partial intestinal obstruction.

The conditions which often simulate mesenteric cysts and must be *differentiated* are (1) Intussusception, (2) ectopic pregnancy, (3) ovarian cysts, (4) volvulus, (5) malignant cysts, (6) tuberculous cysts, especially in children, (7) retroperitoneal growths, (8) hydronephrosis, (9) movable kidney, (10) pancreatic cysts, (11) cysts of the urachus, (12) lipoma of the mesentery, (13) pregnancy, (14) internal hernia, in babies, (15) acute abdominal conditions when cysts are small.

In the *treatment*, the most promising of all procedures is **enucleation**.

**RETROPERITONEAL AND MESENTERIC TUMORS.**—G. Pall (Orvos. hetil. 77. 27 (Jan. 14) 1933) operated upon three cases of retroperitoneal tumors, *i. e.*, (1) an enterocystoma, (2) an endothelial cyst, (3) and a myxolipoma. Retroperitoneal tumors occur twice as often in women as in men. Surprising are the cachectic appearance of the patients and the tendency of the

tumors to recur in spite of the histologically benign appearance. Gastric and urinary tract disturbances are common because of pressure. The tumors are easily confused with ovarian and renal neoplasms and the correct diagnosis is often not made until laparotomy is performed. The only *treatment* is **operation**. Because of the severity of the operation and the length of time it requires, local or spinal anesthesia is preferable to general anesthesia.

**PANCREAS.**—The surgical affections of the pancreas met with in the Johns Hopkins Hospital from 1889 to 1932 have been studied and reviewed by W. F. Rienhoff, Jr and D. Lewis (Bull. Johns Hopkins Hosp 54: 386 (June) 1934). During these 43 years there were admitted to the medical and surgical services 167 cases of pancreatic disturbances, not including cases of diabetes mellitus. Exclusive of 9 cases which were classified on the medical service as cases of pancreatic insufficiency, there were 158 cases of disease of the pancreas among 78,000 cases treated on the surgical service during the period covered by the investigation.

Of these 158 cases, 109 (68.99 per cent) were cases of carcinoma of the pancreas, 20 (12.66 per cent), cases of chronic pancreatitis; 18 (11.39 per cent), cases of acute pancreatitis; 2 (1.27 per cent.), cases of pancreatic abscess; and 7 (4.43 per cent), cases of pancreatic cyst. In 1 case, so-called pancreatic apoplexy was present, and in 1 case, a benign tumor was found.

In the 2 cases of *pancreatic abscess* the mass pointed in the region between the spleen and the left lobe of the liver. As a rule, the mass can be palpated in the left upper quadrant and the tenderness is referred to this region. In both of the reviewed cases **anterior drainage** was accomplished with very good results.

In the case of *pancreatic apoplexy*, death resulted from erosion of the superior pancreaticoduodenal artery. The authors call attention to the fact that the rapid clinical course and the complete necrosis of the pancreas terminating in death were suggestive of a devastating chemical reaction rather than an inflammatory process.

**ACUTE PANCREATITIS.**—*Pathogenesis.*—H. L. Popper (Wien klin Wchnschr 47: 295 (Mar 9) 1934) shows that an inflow of pancreatic secretion into the bile passages can be observed in nearly all acute disorders of the pancreas. If there are disturbances in the discharge at the papilla, a trypsin activation takes place in the biliary passages, and it spreads from the distal, intrapancreatic portion of the choledochus to the pancreas. This tallies with the pressure of the secretion in the pancreatic duct and in the bile duct and makes it understandable why in most cases of pancreatic diseases that come up for necropsy the pancreatic duct shows no changes. It harmonizes also with the close relations between gall-stone disease and pancreatic disorders, since the disturbances in the discharge are caused generally by papillary concretions or by spastic conditions at Oddi's sphincter, which, in turn, are the result of disorders of the gall-bladder or of the bile passages.

The author rejects an etiologic separation between pancreatitis and necrosis of the pancreas. He maintains that they are only different stages and reactions of the same disease process; and the secretory phase of the pancreas, *i e*, the

presence in the cells of larger or smaller amounts of trypsinogen at the onset of the pancreatic disorder, plays an important part in this process. Biliary peritonitis without perforation involves the same pathogenic factors as does acute pancreatitis; however, it can develop only if acute pancreatitis does not, for the two diseases exclude each other to a certain extent. The author believes that his explanations apply to the majority of acute diseases of the pancreas, but admits that a relatively small number of acute pancreatic disturbances must be ascribed to other pathogenic factors.

**Signs and Symptoms.**—Rienhoff and Lewis (Bull. Johns Hopkins Hosp. 54: 386 (June) 1934) state that acute pancreatitis has very characteristic signs and symptoms, but is frequently not recognized because the surgeon fails to consider the possibility of its presence. The indescribable pain, very sudden in onset, the extreme agony accompanying it, which is more severe than that associated with perforated gastric or duodenal ulcer, often comes on after a good meal. The patient lying perfectly quiet and flat on his back presents a marked contrast to the patient suffering from hepatic or renal colic, who tosses and turns constantly. The painful drawn facies, the history of severe epigastric pain, the general condition of shock with a thready and barely perceptible pulse, and the cold, clammy, and often cyanotic extremities, make up a disease picture that can hardly be mistaken. The pain, which usually comes on at night, after a full meal, and is of a stabbing type, is commonly located in the pit of the stomach, but may be felt also in the back and flanks. A peculiar cyanosis of the face and neck, associated with slate-blue patches in the skin of the extremities, occurs practically only in acute pancreatitis. In the cases reviewed by the authors there was uniformly a leukocytosis varying from 9000 to 33,000 and in the great majority the white cell count ranged from 15,000 to 33,000. Most of the patients were between 25 and 50 years of age.

**Treatment.**—All the cases of acute pancreatitis reviewed by Rienhoff and Lewis (*loc. cit.*) were **treated surgically**. The most important surgical procedure in this condition is free exposure of the pancreas with incision through the posterior peritoneum and the capsule of the gland followed by the establishment of drainage down to, and into, the pancreas. If the patient's condition permits, it is well to establish drainage of the gall-bladder and common duct and, if possible, to make certain that the common duct is patent. Of the patients treated in this manner, 55.56 per cent were cured, 5.56 per cent were benefited, and 38.89 per cent died.

Severe acute pancreatitis is treated by O. Mikkelsen (Acta chir. Scandnav. 75: 373, 1934). A review of the literature shows that the treatment still remains almost exclusively operative and that the results of such treatment still show an average mortality of 50 per cent. The **operative treatment** involves an attack either on the pancreas (incision into the capsule and drainage) or on the bile ducts. The author points out that there is no anatomic basis for an operative attack on the pancreas. The pancreas is made up of many small lobules that are separated by thin septums of connective tissue, each enclosing an individual lobule. In order to relieve the pressure tension in the pancreas, it would be necessary to divide the thin layer of connective tissue covering each lobule and that

would not be feasible. Besides, these interlobular connective tissue septums are intimately connected with the glandular tissue, which is always affected at the same time. An operation of this kind is thus apt to cause an increase rather than reduction in the necrosis and intoxication; besides, it implies a not inconsiderable risk of hemorrhage and fistula formation.

The theoretical basis for an operation on the bile ducts is more logical, but the systematic employment of such operative measures in recent years has not lowered the case mortality decidedly; no doubt because these patients are in such a poor condition that they are not able to stand any operative treatment whatever. Recently, a few surgeons have turned to a more conservative treatment, some of them postponing the operation until the "shock stage" is passed, others waiting until all acute symptoms have subsided, after which an operation is performed for gall-stones, when such are found to constitute the underlying cause of the acute pancreatitis. Operation is also performed, of course, if the process goes on to abscess or cyst formation.

During the past 8 years the writers have treated conservatively 39 patients with severe acute disorders of the pancreas. Twenty of these were extremely ill, their general condition being very poor (shock). Three of the 20 patients died, and the remaining 19 were gravely ill but not actually shocked. The diastase value was most often 3000, 4000, 6000 and 12,000; in but 2 cases was this under 2000. Operation was performed only in cases in which gall-stones were ascertained and not until from 1 to 3 weeks after the acute symptoms had subsided. The treatment adopted by the authors consisted of a supply of fluid by mouth, skin and vein, and the use of stimulants and peristaltics. The mortality with this conservative treatment was 7.5 per cent.

**ACUTE INTERSTITIAL PANCREATITIS.—*Diagnosis.***—R. Elman (Surg Gynec Obst 57:291 (Sept) 1933) reports 4 personal cases and reviews 39 collected cases of a disease entity which he diagnoses as acute interstitial pancreatitis. This condition is characterized by induration, swelling, and edema of the pancreas. Hemorrhage, suppuration, and necrosis are absent.

As a rule, there is a history of previous attacks over a period ranging from a few weeks to a number of years. Many patients have complete relief of symptoms between attacks, while others complain of chronic dyspepsia simulating gall-bladder disease. Pain is the predominant symptom. In some cases it is so severe as to cause prostration. In nearly half of the cases with severe pain operation was performed within 24 hours after the onset. In the majority, a diagnosis of biliary colic, perforation of a peptic ulcer, or intestinal obstruction was made before the operation. In only 16 of 35 cases was the gall-bladder found diseased. In no instance was perforation or obstruction discovered. Local tenderness was present in the mid-epigastrium and occasionally also in the left or right upper quadrant of the abdomen. Glycosuria occurred in 6 cases and there was a marked increase of the amylase of the blood in 1 case. Lipase and diastase were found in the urine in 2 cases. In all of the cases the pancreas was examined at operation or autopsy. It was found definitely edematous and sometimes hard and indurated, but showed no hemorrhage or necrosis. In a number of cases, the edema appeared yellow or green, suggesting the presence of bile, but microscopic



studies of the tissue failed to reveal necrosis. The striking finding was a marked infiltration of polymorphonuclear cells into the interstitial tissue of the pancreas.

The author attributes the condition to a reflux of bile from the common duct into the pancreatic ducts.

**Treatment.**—The most effective surgical procedures included, besides **drainage of the pancreas** by **incision**, treatment of the biliary tract such as **bile drainage** with or without removal of the gall-bladder or **cholecystectomy** alone.

**POSTOPERATIVE PANCREATITIS.**—Acute diseases of the pancreas following operations performed in the stomach and duodenum are discussed by R. Euren (*Acta chir Scandinav* 73: 323, 1933). His conclusions on the basis of literature and cases reviewed are as follows:

1 Deep penetration of an *ulcer into the pancreas* necessitates great care in the choice of operation. In cases of ulcer penetrating from the stomach, the danger is considerably less, therefore, **resection** should be performed when possible. In cases of *duodenal* and *pyloric ulcer*, deep penetration may constitute an absolute contraindication to resection. In any case, liberation of the duodenum too far down must be avoided; **gastroenterostomy** or, perhaps, **resection for exclusion** is best.

2 Sharp excision of the base of the ulcer from the pancreas is contraindicated. Because of the danger of an unintentional deep effect, fulguration of the ulcer base remaining in the pancreas is also contraindicated, and unless left entirely alone, the base should merely be carefully **washed out**. In every case it should be **drained**.

3 The treatment of the pancreas in cases of *malignant growth* encroaching upon surrounding tissues remains a problem the solution of which depends chiefly upon the judgment of the surgeon.

4 Such *injuries* as cutting or suturing into the glandular parenchyma, incarceration of the capsule in the suturing of the duodenal stump, and strong traction upon or compression of the parenchyma must be avoided so far as possible.

5 Even in cases of apparently slight lesions of the glandular tissue, the surgeon should always attempt to obtain good drainage and should refrain from primary suture.

**CHRONIC PANCREATITIS.—Symptoms.**—One of the most characteristic symptoms of chronic pancreatitis, which was present in 95 per cent of the cases reviewed by Rienhoff and Lewis (*loc cit*), is a chronic deep, dull, aching and boring pain in the epigastrium which is very difficult to relieve. Nausea and vomiting occurred in 90 per cent of the cases.

**Complications.**—According to C. Rossi (*Policlinico (sez prat)* 41: 323 (Mar. 5) 1934), when pancreatitis is associated with ulcer and with cholecystitis it does not represent a morbid succession of the latter, but a distinct localization of the right abdominal syndrome. As causes of chronic pancreatitis in the literature, the author found chronic intoxications, acute hematogenous diseases, specific chronic diseases (syphilis and tuberculosis), and primary inflammation of the pancreas. He acknowledges the importance of these factors, but maintains that most chronic pancreatitides are secondary to diseases of nearby abdominal organs. In a simple right abdominal syndrome, or in a right abdominal

syndrome associated with cholecystitis or ulcer, the inevitable change in the internal and general function of the pancreas is manifested by the lipolytic power of the serum and by an increase of the glycemic curve during fasting. Thus, the pancreatitis does not depend on the ulcer or cholecystitis, but on the lesions of the right abdominal syndrome, which, in turn, may have produced the ulcer and the cholecystitis. The infection may arrive at the pancreas by way of the lymphatic system, the blood stream, by direct extension or through the omentum. The lymphatic route, however, seems the most logical way of explaining a chronic infection transferred from the appendix to the pancreas.

**Treatment.**—**Operation** was performed in all of the cases reviewed by Rienhoff and Lewis (*loc. cit.*) with only 1 fatality. Procedures which do not specifically lead to drainage of the pancreas are inefficient. If the diagnosis is doubtful, the pancreas may be explored as the chronic inflammation permits repair of the surgical defect in the gland. Of the cases reviewed, **drainage of the gall-bladder** was done in 9, with cure in 4 and improvement in 5. A cure was obtained also by **cholecystectomy** in 1 case, **cholecystectomy with drainage** of the common duct in 2 cases, **cholecystogastrostomy** in 1 case, **drainage of a small cavity in the pancreas** in 1 case, and the **removal of a stone** from the duct of Wirsung in 1 case.

**ACCESSORY PANCREAS.**—L. Ugelli (Polichinico 41:424 (Aug. 15) 1934) presents the following observations based on 106 cases from the literature on accessory pancreas and on 5 cases personally observed. He states that the accessory pancreas is generally found in the thickness of the walls of the gastroenteric tube, from the cardia to the ileocecal valve. The stomach, the duodenum and the first loop of the jejunum were the most frequent sites of the accessory pancreas in the literature and in the author's observations. Accessory pancreas sometimes occurs in the intestinal diverticula. Seldom more than one accessory pancreas is found in a single patient. It may occur at any period of life. It is found equally often in men and in women. It is always congenital and may be associated with other congenital malformations. The nodule of the accessory pancreas is small and hard. Its histologic structure is similar to normal pancreatic tissue, but may have only glandular acini, or typical centroacinous cells, or islets of Langerhans and excretory conduits. It is generally agreed that the accessory pancreas has both internal and external secretion. Little functional value is attributed to this secretion.

The accessory pancreas may be the seat of disease processes involving the principal gland, such as acute necrosis, abscess, chronic inflammation, cystic degeneration, and tumors benign and malignant. In most cases the accessory pancreas is latent and is discovered only at operation or necropsy. Other cases present epigastric pains with frequent radiations to the left hypochondrium, symptoms of biliary calculosis and loss of weight.

The only method of *treatment* is **surgical intervention**. The author concludes that this anomaly is not as rare as is generally believed and that it constitutes a frequent disorder capable of determining various disease symptoms and grave complications.

**PANCREATIC LITHIASIS.—Symptoms.**—A case of pancreatic lithiasis is presented by T. H. Thomason (South. Surgeon 2:281 (Dec.) 1933) with a history of similar attacks of pain in 2 members of the family. A brother, operated on 3 years ago, had had attacks of high epigastric pain, nausea and constipation. He had an extreme grade of movable cecum, with partial obstruction of the hepatic flexure and large mesenteric glands. No pancreatic disease was observed. Symptoms were completely relieved by appendectomy and cecopexy. A cousin, a young boy, also had attacks of pain, and at operation an inflamed gall-bladder with an enlarged, hard pancreas was found. This boy continues to have occasional attacks of pain. The fact that no calculi were demonstrated in the x-ray examination of the author's patient 2½ years ago suggests that previous attacks (*i. e.*, since the age of 5) were due to a recurring pancreatitis, the calculi being a relatively late complication. It is conceivable that developmental defects present in the girl and her brother, and doubtless in her cousin, may have been an etiologic factor.

**Treatment.**—In both children, **appendectomy** and **cecopexy** were followed by prompt relief of constipation of longstanding. The removal of innumerable small calculi throughout the entire gland substance, which are present, is impossible. The future efforts must be directed toward relief of the pancreatitis rather than toward the removal of all the stones. Diabetes looms as ultimately inevitable, as symptoms of an insatiable appetite and craving for sweets, together with a greatly diminished dextrose tolerance, are present. If attacks of pancreatitis continue unabated, complete destruction of the pancreas by fibrosis is imminent, and an existence maintained by **diet** and **insulin** will be all that the future can offer.

**PANCREATIC NECROSIS.—Pathogenesis.**—L. R. Dragstedt, H. E. Haymond and J. C. Ellis (Arch Surg 28:232 (Feb.) 1934) state that death in acute pancreatic necrosis is due in some way to a toxemia arising from the diseased pancreas. Extracts of a necrotic pancreas are exceedingly toxic when they are injected into the abdominal cavities of animals. The nature of the toxic substance is not known. Many investigators have demonstrated that inactive pancreatic juice, when poured into the peritoneal cavity, does not cause inflammation or marked toxemia. The authors verified these observations by draining the main pancreatic duct into the peritoneal cavity by means of a catheter. No symptoms of toxemia appeared, and at necropsy from 5 to 60 days later, no pathological changes other than a few small areas of fat necrosis were discovered.

Other investigators have found that when the trypsinogen in the pancreatic juice is activated, a small quantity of the fluid is rapidly fatal. In an ingenious series of experiments the authors demonstrated that when trypsinogen activated by succus entericus was allowed to drain into the peritoneal cavity freely, no inflammation or signs of toxemia appear, provided the secretion was free from bacterial contamination, whereas, when the same solution was collected and kept free from preservatives or unheated, it rapidly became exceedingly toxic. When, in experiments on 8 dogs, succus entericus was allowed to drain freely into the peritoneal cavity, 7 of the dogs showed no ill effects. When the catheterized pancreatic duct drained its secretions along with the succus entericus, 5 of the 7 dogs

died within 3 days and all showed generalized peritonitis and extensive fat necrosis. In each case bacteria were cultured from the experimentally created jejunal patch. When the activated pancreatic juice was introduced into the peritoneal cavity, no fat necrosis or peritonitis was apparent at necropsy. When the same solution was sterilized by passage through a Berkefeld filter and injected intraperitoneally in quantities as large as 142 c.c., no toxemia or marked fat necrosis was found.

These experiments demonstrate that succus entericus in inactivated and activated pancreatic juice may be poured into the peritoneal cavity without serious consequences, provided the solutions are sterile, but when the solutions are infected, pancreatic juice rapidly provokes toxemia and fat necrosis. The infective organism was usually the *Bacillus welchii*.

Dragstedt and his associates (*loc cit*) have demonstrated that the majority of healthy rabbits and dogs have viable bacteria in their pancreatic tissues. One-half or even the whole of the pancreas may be placed in the abdominal cavity of an animal without serious sequelæ, provided the pancreas is not contaminated. Extracts of autoclaved pancreas have also proved innocuous. When the pancreas is infected, its introduction into the peritoneal cavity rapidly proves fatal. Apparently, then, the digestion of the pancreas in the peritoneal cavity does not produce toxic end-products, but these products develop rapidly when bacteria are present in the tissue so introduced.

The authors conclude that *bacteria* are necessary for the development of toxemia from pancreatic necrosis.

**PANCREATIC CYSTS.—Classification.**—A classification of malignant cystic tumors of the pancreas is outlined by L. Lichtenstein (*Am J Cancer* 21: 542 (July) 1934). In a case reported by the author there was an encapsulated cystic tumor of the tail of the pancreas, the size of a child's head. After an interval of about 5 years the tumor had, in part, undergone carcinomatous change, invading the capsule, and there were carcinomatous metastases in the peritoneum, omentum and liver. A complete clinical record of the case was kept over a period of 6 years. From the data and the autopsy findings the author concludes that the tumor started as a benign cystadenoma.

Lichtenstein divides malignant cystic tumors of the pancreas into 3 classes: (1) essentially solid adenocarcinomata with cysts lined by epithelial cells, (2) large epithelial cysts with carcinoma in the pancreas outside of the cyst wall, and (3) papillary cystadenocarcinoma.

The tumor in the author's case belonged to the third class, consisting of a single, large, encapsulated, and perhaps loculated, cyst with papillary excrescences on its wall, which was not unlike neoplasms seen much more frequently in the ovary.

**Pathology.**—C. Grandclaude, E. Delannoy, and J. Driessens (*Ann d'anat path* 11: 433 (May) 1934) report a case of cystadenoma of the pancreas the size of a child's head which was attached by a pedicle to the tail of the pancreas. **Excision of the tumor without drainage** was followed by recovery. The fluid in the cyst contained albumin, urea, chlorides, phosphates, trypsin, lipase, and a trace of amylase. On microscopic examination, the multilocular cavity was

found to be lined by a flat, excretory type of epithelium. There was moderate evidence of inflammation

A review of the literature showed that 15 cases of pancreatic cyst were discovered in 34,500 autopsies. The condition is most common between the ages of 25 and 50 years and slightly more frequent in females than in males. The authors call attention to the great difference in the suggested classifications of the cysts. They state that macroscopic classifications seem to be of little value. By microscopic examination it is possible to distinguish (1) canalicular cysts, (2) cystadenomata, (3) cystoepitheliomata (malignant tumors to be differentiated from solid epitheliomata which have undergone necrosis), and (4) pseudocysts.

**Pathogenesis.**—Four theories of pathogenesis ascribe the cysts respectively to (1) retention, (2) autodigestion with necrosis, (3) inflammation, and (4) tumor formation. Grandclaude and his associates (*Ibid.*) believe that all true cysts arise from embryonal inclusions. They suggest that true cysts be *classified* as (1) cysts with a single cavity lined with a canalicular type of epithelium, and (2) cysts with multiple cavities, with or without intracystic papillæ.

**Treatment.**—In all of the cases of pancreatic cyst reviewed by Rienhoff and Lewis (*loc cit*) **transperitoneal drainage** through the gastrohepatic and gastrocolic omenta was done and was followed by recovery.

**TUMORS OF PANCREAS.—Adenoma.**—Of 110 cases of new growths of the pancreas reviewed by Rienhoff and Lewis (*loc cit*), in 1 case the tumor was benign—an adenoma of the islands of Langerhans.

**HISTOLOGY.**—The histology of adenoma of the islets of Langerhans is outlined by J. L. O'Leary and N. A. Womack (*Arch Path* 17:291 (Mar) 1934). Five tumors of the pancreas operatively removed were verified as islet adenomas, verifying in each case the preoperative diagnosis of hypoglycemia due to suspected tumor. Although the adenomas varied in size, gross appearance and apparent age, the majority cell type of each was closely allied to the beta cells of the normal islets of Langerhans, but possessed definite tumor characteristics. In only 1 of the 5 tumors was there evidence of a malignant process. The staining reactions of the specific cytoplasmic granules in the majority of tumor cells of each deviated sufficiently from those of the beta cells of normal human islets to lend support to the hypothesis of dysinsulinism. In none of the cases did the histologic picture of the islets of Langerhans of the pancreas containing the tumor indicate the suppression of function that might be expected to parallel the prolonged secretion of excessive amounts of the hypoglycemic hormone.

**DIFFERENTIAL DIAGNOSIS.**—*Hyperinsulinemia* secondary to an adenoma of the pancreas is cited by L. I. Ross and J. M. Tomasch (*Arch Surg* 28:223 (Feb) 1934). The authors report an interesting case of a 33-year-old man who was brought to the hospital by the police as an "alcoholic." He had sustained a contusion over the eye in a fall and, when found, was semi-comatose. As he was still stuporous when brought to the hospital and as the clinical findings were essentially negative, except for a leukocyte count of 16,000, a tentative diagnosis of *alcoholism* with cerebral edema and fracture of the skull was made. When dextrose solution was given intravenously to control the cerebral edema,

the patient suddenly sat up and appeared to be entirely rational. Questioning failed to elicit a history of previous attacks, diabetes, or the use of insulin.

The next morning the patient was again in coma and the blood sugar was 23 mg per 100 c.c. The intravenous administration of dextrose solution was followed by quick recovery, as before. After further tests a diagnosis of hyperinsulinism with hypoglycemia secondary to a tumor of the islands of Langerhans was made. At exploratory operation under spinal anesthesia a purplish cyst-like tumor 2 cm. in diameter was found on the anterior surface of the inferior border of the midportion of the pancreas. This was shelled out. The patient made an uneventful recovery, and has been well ever since. Immediately after the operation the blood sugar was 99 mg. per 100 c.c.

Microscopic examination showed the tumor to be made up of round and polygonal cells suggesting the alpha type of the Bensley terminology.

**Carcinoma.**—In a review of 99 cases of primary carcinoma of the pancreas by N. L. Leven (*Am. J. Cancer* 18:852 (Aug. 1933)), he describes 3 gross and microscopic types: (1) cylindrical-cell carcinoma derived from the epithelium of the duct system, (2) a type derived from the parenchyma of the gland, and (3) a type arising from the islands of Langerhans.

**ETIOLOGY**—Very little is known regarding the cause of pancreatic carcinoma, but chronic pancreatitis, gall-stones, syphilis, alcohol, trauma, and developmental anomalies have been suggested as etiological factors.

Carcinoma of the pancreas is more frequent in men than in women in the ratio of 3.2 or 4.1. It may occur at any age, but is most common between the fifth and seventh decades of life.

**PATHOLOGY**—Carcinoma develops most often in the head of the pancreas. Metastasis first appears in the regional lymph nodes and the liver. Of the 99 cases reviewed, the liver was involved by metastases in 59 and the regional lymph nodes in 50. The more common results from local extension lead to obstruction of the duct of Wirsung with the development of chronic interlobular fibrosis of the pancreas, obstruction of the common bile duct, jaundice, and dilatation of the gall-bladder. In some cases partial obstruction of the duodenum or pylorus may occur. Occasionally pressure on the portal vein produces edema and ascites.

**SYMPTOMS**—The most constant symptoms in the hospital cases studied were cachexia, loss of weight, anorexia, and weakness. The next most frequent symptom was jaundice. In some cases the jaundice was accompanied by pain. Three types of pain were distinguished: (1) a steady, severe, dull mid-epigastric pain radiating to the lower back, (2) a colicky pain in the right hypochondrium, radiating to the right scapular region, and resembling gall-stone colic, and (3) a paroxysmal pain beginning near the umbilicus and resembling that of tabetic crises. Nausea and vomiting occurred in 56 of the hospital cases.

**DIAGNOSIS**—The most significant findings of physical examination were emaciation, jaundice, distention of the gall-bladder, and enlargement of the liver. The gall-bladder was palpable in 14 of the 20 cases presenting jaundice. The liver was enlarged in 81 per cent of the series. A tumor mass other than the liver and gall-bladder was found in 7 cases. In two-thirds of the cases tender-

ness was noted in the epigastrium or over the liver or gall-bladder. In the majority of cases x-ray examination was of little diagnostic aid.

**TREATMENT**—Three types of operations were carried out in the treatment of the cases reviewed by Levin (1) **simple exploration**; (2) **cholecystectomy** and **cholecystogastrostomy**; and (3) **cholecystoduodenostomy**. The maximum survival after operation occurred in cases in which a **cholecystenterostomy** was performed. In the 8 cases in which this operation was done, the average survival period was 14½ months. He considers irradiation to be of doubtful value.

Among the 167 cases of pancreatic disturbances reviewed by Rienhoff and Lewis (*loc. cit.*) there were 109 cases of carcinoma. Of these, 86.21 per cent were in the head of the pancreas, 3.45 per cent. in the body, 3.45 per cent. in the tail, and 6.9 per cent. were diffuse. In no case was an attempt made to remove the carcinoma. In these cases **cholecystogastrostomy** is preferable to cholecystenterostomy, and was found the most satisfactory of all methods used for alleviation of the symptoms.

**PERITONEUM.—SURGERY OF.—Vaginal Approach to Peritoneal Cavity.**—It is pointed out by W. W. Babcock (South Surgeon 3:11 (Mar.) 1934) that in the adult woman the lower peritoneal cavity may be entered, explored and drained in the simplest and quickest way through the vaginal vault. Here the extraperitoneal layers are only a few millimeters in thickness and the peritoneum may be entered by a single thrust of a pair of curved scissors. Such an opening may be readily enlarged by the fingers alone to a size sufficient for exploration of the pelvis and lower part of the abdomen without the division of a single important blood-vessel or the need of a ligature. Not infrequently, a hand may be introduced through such an opening and the lower abdominal structures may be palpated. At the completion of the operation no sutures or peritoneal closure is required, a gauze drain laid through the opening completes the operation. Secondary complications resulting from the vaginal approach are rare, as the integrity of the anterior abdominal wall is not jeopardized. If skillfully done, the vaginoperitoneal section is usually much safer and has a lower mortality than an abdominal section. Against the manifest advantages for the patient, the surgeon must contend against increased difficulties, *i. e.*, restricted operative field, special instruments, and methods of illumination. Adequate training to avoid injury to intestine, bladder, ureter or other important structure and to insure dependable hemostasis is essential.

**CHRONIC PERITONITIS INCAPSULANS.**—S. Hindse-Nielsen (Biblioth. f. læger 126:235 (June) 1934) reviews peritonitis incapsulans on the basis of 50 cases from the literature. He says that it occurs most often in the second and third decades of life, in which the proportion between men and women is 9.3 to 14.2; in the entire material the proportion is 20 to 30. It is a localized, adhesive, fibrohyaline or fibrous peritonitis, which represents an organized remnant exudate after a diffuse peritonitis has originated about a focus in the intestine or mesentery, or is a link in a more diffuse, chronic serositis.

**Etiology.**—The disorder is related to specific infections (tuberculosis, syphilis) and nonspecific infections (pneumococcic infections), and also trauma and cancer.

**Symptoms.**—The symptoms observed in this disorder are constipation, pain, recurring sub-ileus and palpable abdominal tumor.

**Treatment.**—The measures indicated consist in **laparotomy**, with **discission or extirpation of the capsule**, otherwise, **anastomosis** around the pseudocyst or **resection**.

**BILE PERITONITIS.**—E. Melchior (Deutsche Ztschr. f. Chir. 243:458 (June) 1934) states that bile may diffuse through the gall-bladder wall without the existence of an actual perforation. Regurgitation of the pancreatic secretion into the bile tract may bring about an abnormal transfusion of bile. In obstruction of the cystic or common duct and acute inflammation of the wall of the gall-bladder, the latter may "sweat" bile. The toxic effect of bile is due to the rapid absorption of the bile salts, which are toxic for the organism. They become bound up with the red cells and with the muscle cells, among others, those of the heart. The clinical picture of cholemic poisoning is characterized by pronounced adynamia, cardiac weakness and vasomotor paralysis.

A Billi and T. Greco (Clin chir. 10:42, 1934) found that bile in the peritoneal cavity exerts a chemical action and does not produce a true peritonitis. They concluded that the course of choleperitonitis is not favorably influenced by subdiaphragmatic section of the vagi.

**PNEUMOCOCCUS PERITONITIS.**—**Treatment.**—W Budde (Arch f klin Chir 178:308, 1933) states that pneumococcus peritonitis may be considered a general pneumococcus infection, with its primary localization predominantly, but not exclusively, in the peritoneum. When the diagnosis is made with certainty in the first stage, most surgeons avoid operation. In doubtful cases, however, an **exploratory laparotomy** must be done. Exploratory puncture and blood cultures do not always give definite indications. Drainage should be avoided also in exploratory laparotomy. Recently, **polyvalent specific sera** have been made. Their use in large doses seems to have a favorable effect, but in the stage of shock is associated with the danger of serum disease and additional anaphylactic shock. **Optochin** has been especially recommended.

The **operative therapy** of spreading peritonitis is limited, according to J R Buchbinder (Surg. Gynec Obst 59:485 (Sept ) 1934), to removal or closure of a septic focus, aspiration of the exudate and closure of the peritoneum without drainage, and the abdominal wound above the serosa should be drained. All methods of direct surgical attack on suppurative spreading peritonitis, based on alteration of, or interference with, the functions of absorption and exudation, tend to increase the mortality. Drains function in localized peritoneal abscesses, but in spreading processes they not only encapsulate, regardless of the consistence of the exudate, they also provoke residual abscess and increase the diffusion of the infection.

E H Mensing (Am J Surg. 22:478 (Dec ) 1933) states the most important local defensive factors against peritoneal infection are phagocytosis, the formation of a fibrinous exudate, and early localized intestinal inhibition. The



general antibacterial activities are interfered with by anhydremia, demineralization, disturbances of the acid-base balance, anoxemia, and circulatory disturbances. Dehydration and demineralization are treated by means of **normal saline**, **Ringer's** and **Hartmann's solutions**. The anoxemia is treated by correcting circulatory disturbances and by the early use of **oxygen inhalations**. To increase the colloid osmotic pressure of the plasma when shock exists, 6 per cent. **acacia solution** with minute doses of **pitressin** are to be used. **Fluids** may be given by mouth during the time that duodenal intubation with suction is applied. Proctoclysis and enemas are contraindicated in the early cases of peritonitis. **Morphine** is needed to control pain. The splanchnic vasomotor paralysis may be treated in the early stages only by means of small doses of **ephedrine**. Ephedrine also probably lessens "weeping" from the peritoneum and plasma loss into the intestine, and if inhibitory effect upon gut motility is of advantage during the early stages. Inhibition ileus and distention are treated by **duodenal intubation** and the intravenous administration of **hypertonic salt solution**. **Glucose solutions** are especially indicated during the starvation stage. **Fowler's position** is of definite value during the early formative stages. During these stages of peritonitis mild **x-ray** treatment is probably indicated because it raises the antibacterial defense mechanisms. For a mechanical obstruction of the bowel in peritonitis, **enterostomy** is indicated only after the simple method of **duodenal intubation with suction** has been given a trial.

C Vohnout (Rozhl v chir a gynaek 12 114, 1933) uses **bacteriolysate** in the treatment of peritonitis. The substance has no bactericidal effect, but it increases phagocytosis and provokes a leukocytosis. M Gundel and F Sussbrich (Zentralbl f chir 61 306 (Feb 10) 1934) point out that bacteriologic studies of cases of acute appendicitis in the Heidelberg clinic demonstrated the importance of the enterococci and the closely related nonhemolytic strains of streptococci. These organisms recede into the background with the development of an abscess or of postappendical peritonitis. Here the important part is played by *Bacillus coli* and gas gangrene bacilli. They developed a **serum** with antibodies against *Bacillus coli*, gangrene bacilli and enterococci. The technique of administration is as follows. On the termination of the operation, 20 cc of the serum may be introduced into the peritoneal cavity through the rubber tube drain, or it may be administered intravenously, from 20 to 40 cc in 1000 cc of a 5 per cent **solution of dextrose**. For prophylactic treatment, from 20 to 40 cc is introduced intravenously in 500 or 1000 cc of a 5 per cent solution of dextrose. In abscess or peritonitis this dose is repeated on subsequent days.

J G Anderson (Am J Surg 25 521 (Sept) 1934) has been using **autogenous milk vaccine** in the treatment of peritonitis. Injections are given intramuscularly in the gluteal region, from 10 to 25 cc of the vaccine being employed. As a rule, 2 or 3 injections have been given.

#### **STOMACH.—PYLOROSPASM OF NURSLINGS.—Pathogenesis.**

—According to P Boecker (Deutsche. Ztschr f. Chir. 241·377 (Sept 25) 1933), the older anatomic concept of the so-called pyloric hypertrophic stenosis of infants was based chiefly on postmortem evidence. The pyloric tumor was

found to be the result of hypertrophy of the circular fibers of the pyloric musculature, the longitudinal fibers remaining unchanged. The newer functional concept regards the condition as a pylorospasm developing on a neurogenic basis. This concept finds support in observations made in the course of operations on these infants. It was noted that the tumor was located in the antral portion of the stomach. It was, in fact, a prepyloric tumor. The author points to the experience of Lehman, who found that in 10 per cent. of the infants with a palpable tumor, no tumor was found at the operation. Instead, there existed a spasm involving the pyloric and antral portions. This condition, termed by Hurst "*achalasia*," is a functional disturbance in the coordination of the opening mechanism of the pyloric sphincter. For this reason, in Sauerbruch's clinic, these infants are first treated medically in the pediatric clinic. Those who do not respond are turned over to the surgical division. Fifty children were operated on for pylorospasm between 1926 and 1932. Of these, 46 were boys and 4 girls. The mortality was 8 per cent. The author attributes these good results to the simplicity and effectiveness of the Weber-Rammstedt operation.

**Diagnosis.**—Among 34 nurslings with pylorospasm observed by H. Seckel (Jahrb f Kinderh 140 263 (Sept) 1933) in the past 18 months, there were several with peculiar disturbances of the consciousness and with abnormal respiratory movements. This hypochloremic coma, called also *coma pyloricum*, was studied carefully by the author. He mentions the following as the clinical characteristics: (1) disturbances in the consciousness manifested by somnolence, apathy, sopor and coma; (2) respiratory disorders, such as slow and superficial respiration, apnea, hiccup and yawning; (3) muscular hypertonia and nontetanic spasms. The metabolic anomalies are exsiccosis, which is evidenced by loss of turgor, anhydremia and albuminuria; chloropenia, manifested in achloruria and hypochloremia, hyposmosis, which is partially compensated by alkalosis, and azotemia, which, however, is rarely severe and may be absent. In patients without coma, the metabolic changes are similar, but of a much milder degree.

Organic pyloric stenosis in adults and in older children and induced pyloric occlusion in animals are accompanied by essentially the same comatose manifestations and by hypochloremic-alkalotic metabolic disturbances. In adults, gastric spasms and "chloroprivic uremia" predominate. The hypochloremic coma of pylorospasm has to be differentiated from the coma that occurs in alimentary intoxication. The latter form is usually hyperchloremic acidotic and, in contradistinction to the superficial respiration of *coma pyloricum*, it is characterized by forced respiration. For the differentiation of pylorospasm from other conditions characterized by vomiting, examination of the chloride metabolism is recommended.

**PYLORIC HYPERTROPHIC STENOSIS.**—An analysis of 145 cases of *congenital* hypertrophic stenosis of the pylorus was made by H. L. Wallace and L. B. Wevill (Brit M J 1 1153 (June 30) 1934). They state that the ratio of males to females was 6.25 to 1. Fifty per cent. of the patients were first children. The birth weight of the infants was somewhat higher than the normal average for males. The first *symptom* in the majority of cases was vomiting. This began after an average period of 3 weeks. Visible gastric peristalsis was an

almost constant sign, whereas a palpable tumor in the pyloric region was noted before operation in only 24.1 per cent. of the cases.

The operative *mortality* was 24.8 per cent. There was no decrease in the mortality during the past 10 years. The children who failed to survive did not appear to differ significantly in condition at the time of operation from those who recovered. In many of the fatal cases the patient went into shock for no apparent reason and no adequate cause for death could be discovered at autopsy. The time that elapsed between the first manifestation of obstruction and the admission of the patient to the hospital ranged from 3 to 4 weeks.

In reporting the *results of treatment*, J. Oehler (Zentralbl. f. Chir. 61:611 (Mar. 17) 1934) points out that the immediate result of the operation was always a prompt cessation of vomiting. The late results were excellent so far as gastric function was concerned. The general health of these children was satisfactory and there were no developmental disturbances of any kind. The author believes that the results of the operation may be further improved by attention to complete division of the entire involved circular muscular tumor and by what is even more important, the timely operation. The mortality in Oehler's series was 14 per cent.

**Diagnosis.**—*Chronic, hypertrophic stenosis of the pylorus in adults*, according to E. W. Twining (Brit. J. Radiol. 6:644 (Nov.) 1933), is an uncommon benign cause of a prepyloric filling defect. The 3 cases described occurred in the writer's private practice in a series of about 1000 opaque meal examinations. Its interest for radiologists lies in the extreme difficulty of making a differential x-ray diagnosis from other stenosing prepyloric lesions, which it simulates so closely that in nearly all recorded cases a faulty preoperative x-ray diagnosis of carcinoma or prepyloric ulcer has been made. Minor degrees of pyloric hypertrophy are not uncommonly found at operation. Cases showing gross hypertrophy may require surgical treatment, and it is important that a preoperative diagnosis should be made whenever possible. At present the roentgenologic criteria are by no means clear cut. The author presents a detailed study of his 3 personal cases in order to draw attention to the x-ray appearances and to stimulate a closer study of the condition.

**PEPTIC ULCER.—Etiology.**—(G. B. Eusterman and J. G. Mayo (Am. J. Surg. 26:74 (Oct.) 1934) believe that there is apparently adequate evidence to justify the contention that under exceptional circumstances a chronic ulcer of the stomach can have its origin in external, nonpenetrating *trauma* to the epigastric region. In one case, fairly characteristic symptoms of a hemorrhagic gastric ulcer developed following a severe blow to the left epigastric region. The x-rays confirmed the presence of a penetrating ulcer near the lesser curvature 5 months after the injury. Following hospitalization and intensive medical treatment, the lesion disappeared completely and clinical cure resulted. In any case in which a plaintiff claims that a gastric or duodenal ulcer followed external trauma, the physician whose opinion is sought should see that the 4 postulates of Linger and Molineus are satisfied.

A second cause of ulcer is chronic trauma from within. The commonest form of ulcer of this nature is that secondary to congenital (nontraumatic) dia-

phragmatic hernia; foreign bodies in the stomach may also cause ulcer. Such secondary lesions are not indurated, as a rule, and all tend to heal readily following reduction of the hernia or removal of the foreign body.

**Surgical Aspects.**—In discussing the surgical aspects of peptic ulcer, D. P. D. Wilkie (Practitioner 132:417 (Apr.) 1934) states that whereas some peptic ulcers give rise to very few symptoms until their presence is manifested by perforation or hemorrhage, patients suffering from peptic ulcer generally give a very characteristic history of intermittent dyspepsia. It is seldom that an ulcer does not cause attacks of indigestion lasting for several weeks, with intervals of freedom from symptoms lasting for several months. Regularly periodic indigestion is rare in the absence of ulcer. As a rule, the attacks of pain are at first very definite. They last 2 or 3 weeks, come on with clock-like regularity at a definite time after the ingestion of food, and sometimes waken the patient at night. In longstanding cases the symptoms become less severe but more constant. In cases of duodenal ulcer, vomiting is rare; whereas in cases of gastric ulcer, it is common. A history of irregular and capricious pains associated with flatulence suggests that the gastric symptoms have a reflex origin.

In the first or second attacks of dyspepsia of the ulcer type it is justifiable to treat by dietary and medicinal measures without further investigation, but in cases of frequently recurring attacks, with evidence of stenosis or a history of hemorrhage, a fuller investigation is necessary. Lengthening of the attacks, increasing flatulence, a sense of fullness after the ingestion of food, the occurrence of vomiting in the evening or during the night, and a large splashing stomach may indicate a stenosis.

A few years ago there was a strong reaction against surgical measures in the treatment of peptic ulcer and in favor of prolonged medical treatment. This was due to the numerous poor results which followed the indiscreet use of surgery as a quick method of treatment. Today, surgery is employed more frequently, but is used with deliberation and discrimination. The treatment of peptic ulcer is primarily and essentially medical, but there are certain conditions which render surgery necessary, *viz*: (1) stenosis with dilatation of the stomach and gastric stasis, (2) persistent recurrence of symptoms after medical treatment, (3) inability of the patient to carry out adequate medical treatment, and (4) the occurrence of two or more hemorrhages. In cases of gastric ulcer, another indication for surgery is the possibility of the occurrence of malignancy in a large, chronic, and penetrating ulcer. In such cases the operation usually performed is **partial gastrectomy**.

The feature of ulcer which frequently first raises the question of surgery is *hemorrhage*. The general belief that a hemorrhage from a peptic ulcer is rarely fatal is not supported by the evidence. Bulmer found a mortality of 11.5 per cent in cases of hematemesis from peptic ulcer. The death rate is twice as high in the cases of males as those in females. In cases of repeated hematemesis or melena leading to prostration, especially in males, the advisability of surgical intervention should always be considered. Next to **operation**, the most effective method of stopping hemorrhage and maintaining the patient's strength is **blood transfusion**. In the severe case this should always be tried first. Operation

should be advised if it fails. Operation should always be considered when 2 attacks of pronounced bleeding have occurred.

**Surgical Treatment.**—According to J C McCann (New England J. Med. 210:512 (Mar 8) 1934), the rôle of surgery in the management of peptic ulcer should be that of a special therapeutic measure used to cope with complications, or to control those ulcers which fail to respond to medical treatment

The operative technic for treatment of ulcer of the stomach and duodenum is, after 50 years of progress, highly developed and standardized. That point is now reached where a surgeon must individualize each ulcer as viewed at the operating table, and select the operation best suited to each particular lesion. This selection will be done accordingly as the precepts of the school which recommends conservative or radical surgery for ulcer are adhered to. The selection must be made quickly, with a soundness of surgical judgment which equals in importance the accuracy and facility with which the operation itself is done.

The factors which condition the selection of the type of operation best suited for a particular ulcer are 2, *i e*, the extent of the lesion, and its location. The larger, more indurated and calloused is the ulcer, and the farther its location shifts from the duodenum across the pylorus into the stomach, the more extensive will be the operation required. The author's series, though small, bears out this generalization and emphasizes the need for full mastery of all technical methods used in this field, if all situations are to be met adequately.

#### DUODENAL ULCER

##### I *Pyloroplasty*

(A) Partial duodenectomy (Fig 1, A)

(B) Partial duodenectomy and cauterization (Fig 1, B)

(A) Partial duodenectomy is the most conservative operation for ulcer, and is applicable only to simple ulcers. Two factors condition its use: (1) the lesion must be small, in the first half-inch of the anterior wall of the duodenum, and free of all extensive adhesions and deforming cicatrices, (2) the first portion of the duodenum must be sufficiently long, mobile, and wide to permit free delivery from the abdomen. A foreshortened duodenum retracted by a calloused ulcer against the spine, is not suited to this procedure.

(B) Partial duodenectomy and cauterization are used when an anterior wall ulcer suitable for pyloroplasty is associated with a posterior wall, or "kissing ulcer." The latter ulcer, usually exposed after the anterior wall ulcer has been excised, is typically a crater type, located just beyond the pylorus.

##### II *Gastroenterostomy*

(A) Posterior

1. Vertical (Fig 1, II, A<sub>1</sub>)

2. Transverse { Antiperistaltic (Fig 1, II, A<sub>2</sub>).  
Isoperistaltic (Fig 1, II, A<sub>3</sub>)

(B) Anterior with enteroenterostomy (Fig 1, II, B).

(A) Posterior gastroenterostomy, the next least radical operation to pyloroplasty, is used when exploration reveals an extensive cicatrized ulcer of the duodenum which foreshortens, contracts, or obstructs the duodenum. A direct

attack upon such extensive pathology by a plastic operation would not be feasible. An indirect drainage operation to induce healing of the ulcer is offered by gastroenterostomy.

(B) Anterior gastroenterostomy with enteroenterostomy is used for the same type of lesion as above, when technical factors make a posterior anastomosis inadvisable. Such factors are a narrow costal arch with a high lying stomach, extreme deposits of fat in the mesocolon, or foreshortening of the mesocolon.

DUODENAL ULCER 91 OPERATIONS.				
TYPE OF OPERATION	NO	TYPE ULCER	TECHNICAL FACTORS	DIAGRAM
<b>I PYLOROPLASTY</b>				
A PARTIAL DUODENECTOMY	5	SMALL ANT. WALL ULCER 2 OF PYLORUS	MOBILE DUODENUM NO CICATRICES	
B SAME AND CAUTERIZATION	3	POSTERIOR WALL KISSING ULCER		
<b>II GASTRO-ENTEROSTOMY</b>				
A POSTERIOR		CICATRIX		
1 VERTICAL	59	DEFORMITY		
2 TRANSVERSE	8	CRATER		
3 ISOPERISTALTIC	4			
B, ANTERIOR WITH ENTERO-ENTEROSTOMY	3	SAME		
<b>III CLOSURE PERFORATION</b>				
A SIMPLE CLOSURE	4	CICATRIX DEFORMITY PERFORATED	OVER 6 HOURS POOR RISK	
B CLOSURE AND GASTRO-ENTEROSTOMY	3	SAME	UNDER 6 HOURS GOOD RISK STENOSIS PYLORUS	
<b>IV DIVINE EXCLUSION</b>				
	2	CICATRIX DEFORMITY PENETRATION HEMORRHAGE	POOR PROTECTION FROM G.E. OPEN PYLORUS POOR RISK FOR RESECTION	

Fig 1.

(J C. McCann New England J Med)

### III Closure of Perforated Ulcers

(A) Simple closure (Fig 1, III, A)

(B) Closure with gastroenterostomy (Fig 1, III, B)

The most serious type of duodenal ulcer is one which has perforated into the peritoneal cavity. There were 8 perforated ulcers in the author's series, all located in the duodenum within a few centimeters of the pylorus. A calloused indurated area 2 or 3 cm across usually surrounded the point of perforation. The problem which confronts the surgeon at the time of operation is whether simple closure shall be done or whether a gastroenterostomy is necessary in addition to the closure. In making a decision, McCann was influenced by 3 factors: (1) the length of time that elapsed between perforation and operation—after 6 hours a gastroenterostomy was not done, (2) the risk of operation, as determined by the age and general condition of the patient, and (3) the degree of obstruction in the duodenum caused by the closure of the perforation.

IV. *Devine Resection by Exclusion*

The next most complicated group of duodenal ulcers is the type of cicatricial lesion described above which is complicated by hemorrhage or threatened perforation. Such a lesion, associated with a patulous pylorus, would not be protected adequately by gastroenterostomy. After a gastroenterostomy, enough irritating chyme would pass through the patent pylorus to irritate the ulcer and prevent its healing, and possibly result in perforation or hemorrhage. These dangers are not, however so imminent as to warrant extensive resection for all such lesions. A satisfactory compromise with adequate protection is afforded by the Devine operation or resection by exclusion.

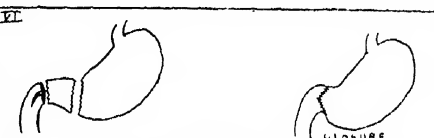
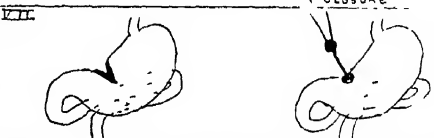
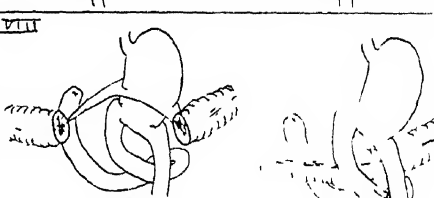
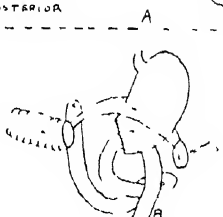
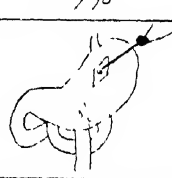
GASTRIC ULCER 12 OPERATIONS				
TYPE OF OPERATION	NO	TYPE	TECHNICAL FACTORS	DIAGRAM
<b>I</b> PYLOROPLASTY	1	SMALL ANTERIOR PREPYLORIC	MOBILE DUODENUM NO CICATRICES	<b>V</b> SEE <b>I</b>
<b>VI</b> PYLORECTOMY BILLROTH T (HORSLEY)	2	DISTAL HALF ANTRAUM		<b>VI</b> 
<b>VII</b> EXCISION (CAUTERY) AND GASTROENTEROSTOMY	1	ULCER AT ANGLE OF STOMACH	SMALL ULCER	<b>VII</b> 
<b>VIII</b> PARTIAL RESECTION A POLYA	2	PROXIMAL HALF ANTRAUM GASTRIC AND DUODENAL ULCER		<b>VIII</b> 
<b>B</b> BILLROTH II	1	SAME	LARGE DILATED FUNDOUS WIDE RESECTION SMALL POUCH	
<b>IX</b> TRANSGASTRIC CAUTERY AND GASTROENTEROSTOMY	1	ULCER FUNDOUS POSTERIOR WALL		<b>IX</b> 
<b>X</b> GASTROENTEROSTOMY HIGH CARDIAC ULCER	4		BETWEEN CAUTERY OR RESECTION	<b>X</b> SEE <b>II</b>

Fig 2

(J C McCann New England J Med)

## GASTRIC ULCER

As the location of an ulcer shifts from the duodenal to the gastric side of the pylorus, the variety and extent of the operative procedures necessary to cope with it increase. This is due to the necessity of removing or destroying all chronic gastric ulcers, as 10 to 15 per cent probably undergo malignant change

### V. *Pyloroplasty:*

This very conservative procedure is applicable in the very few instances in which the gastric ulcer is located on the anterior wall of the stomach close to the pylorus. The author could use it for only 1 gastric ulcer in his series.

### VI. *Pylorectomy Billroth I:*

Ulcers located in the distal half of the antrum, but too far proximal from the pylorus to be suited for excision and plastic repair, are best treated by pylorectomy. This operation, as devised by Billroth, consists in removal of a sleeve of tissue from the stomach between the pylorus and a point proximal to the lesion, and uniting the stomach and duodenum in direct continuity.

### VII *Local Excision (Cauterization) and Gastroenterostomy:*

Ulcers located higher on the lesser curvature near the incisura angularis are more amenable to direct surgical attack than ulcers located elsewhere in the stomach. Formerly a sleeve resection of tissue containing the ulcer was made from the whole circumference of the stomach, and the open ends anastomosed in direct continuity. This operation has been abandoned because of the subsequent disturbance in the motility of the stomach, and the occurrence of hour-glass contractures at the suture line. Excellent results have been obtained by local excision of such an ulcer and the addition of a gastroenterostomy.

### VIII *Partial Gastric Resection*

(A) Polya (Reichel and Balfour) (Fig. 2, VIII, A).

(B) Billroth II (Fig. 2, VIII, B).

Frequently an ulcer will be so situated in the proximal half of the antrum that it cannot be removed by the methods described above. For an extensive lesion in the proximal half of the antrum, or for an antral lesion associated with a duodenal ulcer, both of which are to be removed, a more adequate resection becomes necessary.

### IX *Transgastric Cauterization and Gastroenterostomy*

As the site of the ulcer moves from the angle of the stomach into the poorly accessible parts of the stomach, as on the posterior wall of the fundus, the danger of radical resection far outweighs any potential danger from the lesion itself. More conservative methods may be used to cope with them. An ulcer of the posterior wall of the fundus may be excised, or may be destroyed by transgastric cauterization, through an incision in the anterior wall of the stomach. Either procedure should be followed by a gastroenterostomy.

### X *Gastroenterostomy for Ulcers of Cardia*

The ulcers most difficult of access are those located high in the cardia near the esophagus. Here, they are not resectable or amenable to destruction by cautery with any degree of safety. However, this type of lesion will respond satisfactorily to simple gastroenterostomy. The literature conveys the impression that ulcers located proximal to the point of gastroenterostomy will not heal satisfactorily. This has not been the experience of many competent observers. These ulcers of the cardia have responded satisfactorily to gastroenterostomy in 70 per cent. of cases. In very intractable ulcers of this type, Balfour suggests jejunostomy for complete rest of the stomach.



## GASTROJEJUNAL ULCERS

This group represents secondary lesions initiated by and developing after an operation for a primary ulcer. A gastrojejunal ulcer is a new and distinct ulceration at the site of a gastrojejunal anastomosis, and a gastro jejuno colic fistula is the complicating erosion of such an ulcer into the colon. The management of such lesions presents the most complicated technical problems in the surgery of peptic ulcer. Depending upon the conditions present, the steps consist essentially in disconnecting the gastroenterostomy, excising the ulcer and doing such a type of gastrointestinal anastomosis as is indicated.

XI. *Disconnection of Gastroenterostomy and*

(A) Pyloroplasty

(B) Roux en Y anastomosis.

(C) Polya or Billroth resection

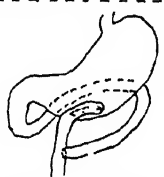
GASTRO-JEJUNAL ULCER 2 OPERATIONS				
TYPE OF OPERATION	NO	TYPE ULCER	TECHNICAL FACTORS	DIAGRAM
XI DISCONNECTION GASTROENTEROSTOMY AND A PYLOROPLASTY	1	JEJUNAL ULCER SMALL ULCER DUODENUM	MOBILE DUODENUM NO CICATRICES	XI SEE I
B ROUX EN Y	1	JEJUNAL ULCER JEJUNO-COLIC FISTULA OBSTRUCTED PYLORUS DANGEROUS RISK	DUODENUM FIXED  DRAINAGE NECESSARY	
C POLYA	0	SAME		
				SEE VIII A

Fig 3

(J C McCann New England J Med)

Occasionally it will be found after disconnecting a gastroenterostomy and excising the jejunal ulcer that the duodenal ulcer for which the anastomosis was originally made has healed. Nothing further need be done except to close the defects in the stomach and jejunum. Subsequently, the patient's diet should be regulated. Sometimes after disconnection of the anastomosis, a small ulcer of the duodenum will be found which is suitable for excision.

Occasionally a Roux en Y operation will solve a difficult problem after an old anastomosis has been disconnected. The author used it on a 55-year-old man with a gastrojejunal ulcer and jejunocolic fistula, who was admitted to the hospital following a severe hemorrhage. There was a persistent complete pyloric obstruction, for which the original gastroenterostomy had been done. After resection of the anastomosis and ulcer, there was absolute need for further surgery, but it was apparent that the patient would not survive a partial gastrectomy. A Roux en Y anastomosis was made as quickly as possible.

*Accessory Operations*—There are two operations which do not aim directly at the control of an ulcer itself, but which are of great value in meeting emergency situations which occasionally arise in the general surgical management of peptic ulcer. These are jejunostomy and enteroenteroanastomosis.

## XII. Jejunostomy.

Witzel introduced the principle of suturing a catheter into the gastrointestinal tract in 1891. McCann used it once to improve the condition of an emaciated patient who came to the hospital vomiting excessively from a malfunctioning gastroenterostomy performed elsewhere. Balfour recommends it for large ulcers high in the cardia, or for large inflammatory gastrojejunal ulcers which cannot be safely resected. It might also be used for late vomiting after gastroenterostomy, due to closure of the stoma from inflammatory edema of the anastomosed stomach and jejunum, and mesocolon.

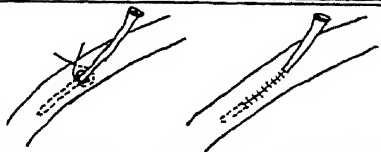
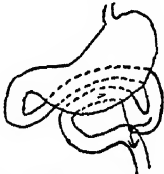
ACCESSORY OPERATIONS			
TYPE OF OPERATION	NO	TYPE	DIAGRAM
XII JEJUNOSTOMY	2	POOR RISK VICIOUS CIRCLE	
XIII ENTERO-ENTEROSTOMY	1	VICIOUS CIRCLE	

Fig. 4.

(J C McCann New England J. Med )

## XIII Enteroenteroanastomosis

This operation was first introduced by Braun in 1892, who used it to unite the afferent and efferent loops of a long loop gastroenterostomy. It is also occasionally of value between the two loops of a short loop posterior gastroenterostomy when the vomiting of a vicious circle appears. Although this complication has almost disappeared with the short loop anastomosis, yet it occasionally does develop. If due to the mechanical conditions of the anastomosis and not to inflammatory edema at the stoma, it may be corrected by enteroenterostomy.

GASTROENTEROSTOMY.—The *causes of unsatisfactory results* of gastroenterostomy are commented upon by A. Grevle (Norsk mag. f. laegevidensk. 95: 1113 (Oct.) 1934). The author's material comprises 78 patients, observed for from 1 to 16 years, who have answered his questionnaires. Fifty-one are cured. In 20 of the remaining 27 cases with more or less marked disturbances, he made clinical and x-ray examinations and presents the results in detail. He finds that the anastomosis lies too far to the left in practically all cases. Except in 2 instances, emptying occurs by both pylorus and anastomosis. In 2 cases the acidity is increased, in some it is unchanged, and in one-half of the cases there is anacidity. A peptic ulcer was revealed in a woman with anacidity. The best results are seen in elderly patients and the poorest in those aged between 15 and 20. There is no evidence that the duration of the disorder influences the results of the operation.

The *fat content of feces after gastroenterostomy*, according to I Snapper (Geneesk. Gids (Apr.) 1934), generally increases. He states that this is due to an excessively rapid passage of the chyme through the jejunum as a result of the operation, so that there is too little time left for the resorption of the fat. In some patients this chronic loss of fat in the feces seems to be the cause of emaciation and fatigue. Exceptionally it may be necessary in these cases to undo the gastroenterostomy. If, however, true fatty feces and fatty diarrhea occur after gastroenterostomy, there is always a gastrojejunal fistula. A peptic ulcer, which often develops in the jejunum after gastroenterostomy, may cause adhesions to the colon. As a result, there is a communication between the jejunum and colon and, consequently, an open connection between the stomach, jejunum and colon. The characteristic symptomatology of the condition includes fat diarrhea, eructation of fecal matter and roentgenologic filling of jejunum and stomach after administration of a barium enema. The author describes 3 patients presenting the characteristic symptoms of gastrojejunal fistula, one of whom showed symptoms of tetany. Operation of the gastrojejunal fistula in all cases gave immediate disappearance of fat from the feces, and the general condition of the patients improved rapidly. One patient developed new duodenal ulcers after the fistula had been closed. Several operations took place after this, the last terminating in death.

*Endoscopic Study of Gastroenterostomy*—F Moutier (Presse méd 42 653 (Apr 21) 1934) made an endoscopic study in 26 cases in which gastroenterostomy had been done from 3 to 20 months previously, to determine the cause of the complaints which so frequently follow that operation. In 4, the gastroenterostomy was done for gastric ulcer, in 19, for duodenal ulcer, in 1, for a stenosing periduodenitis, in 1, for gastric atony with retention, and in 1, for an antral neoplasm.

Endoscopic examination following gastroenterostomy is difficult because insufflation of the stomach with air is often poorly tolerated. Not only the shape, but also the capacity of the stomach is changed. Orientation is usually difficult because the stomach is twisted. There is a change in its longitudinal axis as well as in the shape of the antrum, due to the distortion of the position of the posterior wall by the operation. The effect of the twisting of the stomach is further distortion of the very important longitudinal folds which are essential for orientation. The distortion of the entire stomach may be so pronounced that the posterior gastric wall passes the median line and the gastroenterostomy stoma appears to be on the anterior wall. The pylorus may or may not be visible, or may be seen in the same field as the gastroenterostomy stoma. There may be a sacculum of the greater curvature which may cover and obstruct the view of the gastroenterostomy stoma. The gastroenterostomy stoma may be so changed in shape that it may be mistaken for the closed pylorus. Invagination of the jejunum through the gastroenterostomy stoma may increase the distortion of the picture. An associated perigastritis and retraction of the mesentery, with traction on the antrum, leads to further diminution of the size of the already reduced antrum.

The contents of the stomach after gastroenterostomy vary. The stomach may be empty or may contain bile, blood, or mucus. When once orientation in the stomach is obtained, the gastroenterostomy stoma should be localized. This may be very difficult, not only because of the reasons cited, but also because the stoma may not be found where it was localized previously at x-ray examination. Bile or gas exuding from it may aid in its localization.

In some cases there may be found a nonulcerative gastritis characterized by marked hypertrophy of the mucosal folds with deep troughs between them and abnormally broad crests. This mucosal hypertrophy may progress until the classical "*état mammelonné*" results. There is usually a marked congestion of the mucosa, and there may be small patches of mucus which progress to an extensive myxorrhoea. The process may advance to the inflammatory condition described by Konjetzny and continue until there is found, first, a superficial erosion and, later, a true erosion. The ulceration may be at the new stoma or elsewhere, or the original ulcer may be still active.

Symptoms following gastroenterostomy may, therefore, be due to new pathological changes, persistence of the old lesions, or mechanical malfunction of the gastroenterostomy stoma. The latter may be due to faulty placing, too small size, or cicatricial stenosis of the stoma, herniation of the small bowel into the stoma, peristomal inflammatory swelling, or peristomal adhesions.

The author concludes that the high incidence of gastrojejunal symptoms following gastroenterostomy is due to spread of the inflammatory process from the tissues in which the operation is performed, which is favored by the surgical intervention, and to the fact that the operation is not physiological. He states that when no pathological changes are seen on endoscopic examination, it may be assumed that the symptoms are of neuropathic origin.

**Treatment of Hemorrhage.**—The treatment of profuse bleeding from the stomach and duodenum is outlined by R. S. Aitken (Lancet 1 839 (Apr 21) 1934), who reports a study of the records of 63 such cases which were treated at the London Hospital in the period from 1929 to 1933. In 31, strictly medical treatment was given; in 11, medical treatment with the addition of blood transfusion; and in 22, surgical treatment.

Of the 31 patients given strictly medical treatment, 17, with an average age of 51 years, died, and 14, with an average age of 41 years, recovered. When 1 patient 74 years old, 3 patients with malignancy, and an infant 2 days old are excluded, there remain 26 patients given medical treatment alone, 12 of whom died of gastric or duodenal hemorrhage while under the treatment.

In the 11 cases treated medically with the addition of **blood transfusion** there were 3 deaths. The average age was 41 years.

In the cases treated surgically there were 7 deaths and the average age was 45 years. In all of the cases in this group the operation was performed to obtain hemostasis.

From this study the author draws the following conclusions:

- 1 A distinction should be made clinically between grave cases and those less severe. Recurrent bleeding is often, but not always, grave. Cases in which the red cell count falls below 2,000,000 or the hemoglobin decreases below 40 per

cent. (on a scale on which the normal is 100), will usually be grave. However, the distinction should be based on consideration of the clinical picture as a whole.

2. The less severe cases should be treated according to accepted medical principles.

3. The grave cases should be treated medically, with the patient in **bed**. Sufficient **morphine** should be administered to insure complete rest, and a **transfusion** of about 500 c.c. of blood should be given, without moving the patient from his bed, after careful cross-grouping.

4. If further bleeding is indicated by subsequent hematemesis or a rising pulse rate, the transfusion should be repeated once or twice within from 24 to 48 hours or when necessary.

5. If bleeding still continues and the patient's condition deteriorates, operation should be undertaken promptly and another transfusion given. The operation should probably be restricted to the minimal procedure necessary to find and secure the bleeding point.

**PERFORATED PEPTIC ULCER.**—Eliason and Ebeling (*loc cit*), in a review of 546 duodenal and 183 gastric lesions, found that 11 per cent of the duodenal ulcers and 7.6 per cent of the gastric ulcers had perforated. Of the 74 patients with perforations, only 1 was a female. Frank hematemesis occurred in 9 of 54 cases of ulcer. Perforation occurred with equal frequency throughout the year. Thirty of the perforated ulcers were closed with drainage of the peritoneal cavity, and 3 were closed without drainage. Simple closure was done, therefore, in 33 (47 per cent) of the cases. In many, the ulcer was cauterized prior to closure. Gastroenterostomy was added to simple closure in 15 cases with drainage and in 9 without drainage, being performed, therefore, in 24 (34 per cent) of the cases. Drainage alone was done in 10 cases in which the condition of the patient, the presence of a localized abscess, or failure to find the perforation made this procedure necessary.

The gross *mortality* in the 74 cases of perforated ulcer was 45.9 per cent. As has been reported by others, the mortality of perforated lesions becomes progressively higher with an increase in the time elapsing between the occurrence of the perforation and surgery.

Fifty per cent of the deaths in the cases reviewed were due to peritonitis, 14 per cent to pulmonary complications, and the remainder to cardiac failure, intestinal obstruction, and unknown causes.

**Diagnosis.**—The importance of the x-ray examination of the abdomen in acute abdominal conditions in patients with a positive Jobert's sign (disappearance of the hepatic dullness on percussion in the liver area) is emphasized by Fernandez A. Saralegui and G. Belleville (*Semana méd.* 2:936 (Sept. 27) 1934). The sign indicates the presence of spontaneous pneumoperitoneum, the typical syndrome of perforation of a hollow viscus, and its x-ray verification indicates the emergency of an immediate surgical intervention on the patient. Two cases of spontaneous pneumoperitoneum by perforation of ulcers of the anterior aspect of the pylorus, with atypical and classic clinical pictures, respectively, are reported. In both cases the results of the x-ray examination of the abdomen that confirmed the diagnosis of pneumoperitoneum, based on the pres-

ence of a positive Jobert's sign, were the basis for the decision to perform an immediate operation, which saved the life of the patients.

In the *localization* of perforated peptic ulcers, O. M. Nisbet (Northwest Med. 33: 238 (July) 1934) recommends **methylene blue** in abdominal emergencies in which a perforated peptic ulcer is suspected. The operating time is definitely shortened. There should be less manipulation of the viscera if the distribution of the dye is observed. The dye is of definite value in a differential diagnosis. The diameter of the perforation is easily determined and, when the perforation is sealed by a plastic exudate, the stain shows the site of the original lesion and also whether or not further plastic surgery is required. During the past 5 years the author has had 17 cases of perforation. In some of these the diagnosis was obscured by the inability of the patient to give an accurate history.

**Treatment.**—The study made by Eliason and Ebeling (*loc. cit.*) demonstrates very definitely that **gastrojejunostomy** added to a **simple closure** does not affect the mortality if the procedure is carried out in selected early cases.

The findings indicate also that medical treatment has the lowest immediate mortality in cases of acute exsanguinating hemorrhage from a bleeding gastric or duodenal ulcer, and that in cases treated by the average surgeon, the immediate mortality is lowest when the treatment consists in **simple closure with adequate drainage of the peritoneal cavity plus gastric drainage by means of a Jutte tube, adequate pulmonary exercise** and the administration of **sufficient fluid**.

**TUBERCULOSIS OF STOMACH.**—M Nedelec (Arch franco-belges de chir. 34.76 (Feb.) 1934) discusses tuberculosis of the stomach, especially from the pathological aspect. He reports the case of a patient with pyloric obstruction due to an inflammatory mass for which a **posterior gastroenterostomy** was done. During the first month after the operation there was considerable improvement, but later the epigastric pain, weakness and diarrhea recurred. At a second laparotomy, the **pylorus was removed**. The inflammatory mass was found to have disappeared, leaving only an ulcer with fibrosis, but enlargement of the regional lymph nodes was still present and the duodenal mucosa was thickened and involved by tuberculous granulations. The diagnosis was made by histological examination of the tissue. The patient died 48 hours after the second operation.

Tuberculosis of the stomach is rare. It is most frequently seen after the age of 35 years. It is manifested clinically by the symptoms of a rapidly progressing stenosis of the pylorus. While cold abscess of the stomach has been reported twice and there are descriptions of a diffuse form of gastric tuberculosis resembling linitis plastica, the common pathological types are the ulcerating and the hypertrophic. The author discusses the frequency, symptoms, pathology, and diagnosis of these two forms. He concludes that the findings are easily confused with those of gastric ulcer or carcinoma. The diagnosis is generally made by histological examination of the removed tissue. A clinical diagnosis is exceptional.

Nedelec reviews 57 surgically treated cases collected from the literature. He states that **resection of the pylorus** is probably the procedure of choice.

**TUMORS OF STOMACH.—Neurinoma.**—According to most statistics, benign tumors of the stomach are relatively uncommon, constituting only from 1 to 2 per cent. of all gastric tumors. They may originate from any of the tissues of the stomach or from aberrant tissue in the stomach wall. Benign tumors originating from the nerve tissue are the least common.

G. Bendandi (Ann. ital. di chir. 13:241 (Mar. 31) 1934) reports a case of neurinoma of the stomach in a woman 29 years of age. The clinical syndrome consisted essentially of 3 hemorrhages from the stomach. Two years after the last attack, when the patient was apparently in a normal state of health, she was subjected to a routine fluoroscopic examination. This revealed a rounded filling defect in the center of the lesser curvature of the stomach. The emptying time of the stomach and the findings of all other tests were normal.

At laparotomy a tumor the size of a hen's egg and weighing 55 grams was resected. The mucosal covering was bright red except for 2 scars. The surfaces of sections of the mass showed zones of tissue involved by hemorrhage next to relatively compact tissue of a whitish hue. The portion of the tissue involved by hemorrhage was spongy. A dense capsule encircled the mass. The serosa of the stomach was normal.

The findings of histological examination of the tumor are described in detail and shown by photomicrographs. There were 3 characteristic changes: (1) nuclei arranged parallel on a thin layer of connective tissue which formed an unusual palisade-like structure, (2) masses of nuclei forming fan-like and vortex-like figures; and (3) zones of microcystic degeneration and other myxomatous changes. Considerable vascular dilatation and cellular infiltration were also present.

The author tabulates the principal characteristics of 25 similar cases which he found in a review of the literature, and on the basis of these and his own case discusses the frequency, sex incidence, location, size, and symptoms of gastric neurinomata. As is true of most benign tumors, the clinical symptoms of gastric neurinomata depend upon the complications.

Bendandi suggests classifying gastric neurinomata as follows:

1. Extragastric pedunculated, without gastric symptoms.
2. Intragastric (a) pedunculated, with or without symptoms; (b) intramural.

**Cancer.**—**PROGNOSIS.**—H. K. Gray and D. C. Balfour (Am. J. Cancer 22:249 (Oct.) 1934) point out that, in its various forms, cancer of the stomach may be considered either one of the most hopeless or one of the most curable types of cancer. The increase in the incidence of malignant processes of the stomach is undoubtedly partially the result of those achievements in preventive medicine which have increased the span of life. Because of progress in the diagnosis, cancer of the stomach is being recognized in its earlier stages, and on this depends the possibility of cure. Experience has now shown that a malignant process of the stomach may be curable if diagnosed early enough in its growth. Permanent cures are rare in relation to the number of cases encountered. If, however, the fact that early removal is the only known method of cure were emphasized more, a larger number of persons would undoubtedly submit promptly to

examination and operation, with consequent increase in the number of satisfactory results. In cancer of the stomach, death will inevitably occur within a period of months if the disease is not interrupted in its course. The authors feel that exploration is warranted in any case of cancer of the stomach, unless it is clearly incurable because of distant metastasis or unless the lesion itself is definitely inoperable, as evidenced by x-ray examination.

**TYPES**—J. R. Goyena and H. J. d'Amato (*Semana méd.* 2:745 (Sept. 13) 1934) report 28 cases of gastric cancer and conclude that atypical forms are frequent (36 per cent). The febrile acute form gave a frequency of 7 per cent. The fever in this form is, as a rule, of a continuous and irregular type and may not be high. The febrile acute form may be interpreted, from the anatomopathologic point of view, as an association of gastric ulcerous tumors and a permanent infection. Whether the infection is the cause or the consequence of the ulcers cannot be asserted.

The most frequent atypical form of gastric cancer is the *juvenile form* (14 per cent.) On account of its high frequency, this form may be suspected even in patients less than 30 years of age. In the authors' group of the juvenile form, the two sexes were affected in the same proportion (7 per cent each in women and in men). This observation is not in agreement with the opinion of Mentier, who states that this form is more frequent in men than in women. Juvenile cancer develops at an earlier age in women than in men and its evolution is more rapid and grave in female than in male patients. If anachlorhydria is of diagnostic importance in gastric cancer, hyperchlorhydria or even the mere presence of free hydrochloric acid in the gastric secretions, is not a negative sign for the diagnosis of gastric cancer. Marked hyperchlorhydria may be present in cases of pure gastric cancer without previous symptoms of peptic ulcer.

The mental condition of patients suffering from the *psychopathic form* is probably due both to anemia caused by a tumoral vasoconstriction and resulting in a diminished cerebral blood supply, and to the impregnation of the nervous cells by gastric toxins of tumoral origin. The form of gastric cancer with conservation of the appetite may develop in patients at any age, and not necessarily in patients with the juvenile form, as Le Noir and Riege say. The appetite of patients with gastric cancer may change under various influences of mechanical or psychic nature and these influences may appear in the course of the disease and cause a transformation of the anorectic type into a type having normal appetite or even bulimia.

**DIAGNOSIS**—U. Maes, F. F. Boyce and E. M. McFetridge (*Ann Surg* 98:619 (Oct.) 1933) state that no symptom is constantly present in cancer of the stomach, and the diagnostic difficulties are greater the earlier the patient seeks medical aid. There is no specific laboratory test for the condition. The safest diagnostic plan is to attribute to cancer, until cancer is ruled out, any indigestion which develops after middle age, acutely or insidiously, in a person who has been well previously.

**X-ray Diagnosis**—It is pointed out by B. R. Kirklin (*Radiology* 22:131 (Feb.) 1934) that in gastric ulceration, when the lesion is on or near the lesser curvature in the vertical portion of the stomach, the ulcer crater is seen roent-



genoscopically under palpatory pressure as a crescentic shadow, with its convexity directed outward, and that the term "meniscus" is aptly applied to it. When the lesion is on the lesser curvature distal to the angular incisura, the base of the crater bends with the wall and the meniscus is concave above. If the ulcer is on the posterior wall, the crater appears, under manual pressure over the stomach, as a dense, irregularly rounded shadow encircled by a transradiant zone, which corresponds to the elevated border. At the Mayo Clinic, in every surgical case in which these manifestations are elicited, an ulcerating carcinoma has been found at operation.

The author believes that, although the meniscal form of the crater as seen in typical cases is important, it seems to him that the slightly raised, overhanging border is even more significant. When the pressure necessary to demonstrate it is exerted over a lesion of this character on the lesser curvature, the crater filled with barium is separated from the barium in the stomach by a clear zone, representing the approximated overhanging border of the ulcer. Similarly, when the lesion is on the posterior wall, the marginal ridge surrounding the crater is depicted as an encircling transradiant zone. In either instance the zonal defect is quite as striking as the shadowed crater and distinguishes the lesion from benign ulcer, which seldom has a raised or overhanging border. Another mark of the meniscus crater is its slowness in emptying under pressure, and for this the marginal shelf is also responsible.

To demonstrate these lesions and determine their character, x-ray examination under manipulation is indispensable. Inspection should begin when the first swallow of barium enters the stomach, and the mixture should be distributed over the gastric walls by palpatory pressure to exhibit the entire mucosal relief. By a downward stroking pressure of the examiner's hand, the meniscus complex of the crater and the encircling ridge can be seen clearly above or between the outspread fingers. The complex is demonstrable not only when the lesions are moderately large, but also when they are quite small.

*Carcinoma of the cardia* is much more frequent than is commonly believed. Every case with clinical findings suggesting such a lesion should be carefully studied roentgenologically by a careful technic. Multiple examinations with the use of various modifications of technic may often aid in the differentiation of lesions. The x-ray findings must be correlated with the clinical history and other findings.

W. H. Stewart and H. E. Illick (*Am J Roentgenol* 32:43 (July) 1934) describe the following 10 x-ray signs of carcinoma of the cardiac portion of the stomach: (1) Dilatation of the lower esophagus; (2) abnormal retention of barium in the lower esophagus; (3) the passage of the barium through the esophageal orifice in a continuous stream; (4) narrowing of the esophagus and unchanging canalization through the tumor; (5) infiltration preventing normal movements of the lower esophagus; (6) a mass visible in a gas bubble; (7) a mass visible after the first swallow of barium and after distention of the stomach by the full meal; (8) forking of the barium over a mass; (9) gastric hypermotility; and (10) esophageal antiperistalsis.

The most important conditions to be *differentiated* are cardiospasm, diverticulum of the lower esophagus, varices, extrinsic lesions producing pressure on the esophagus and cardia, hernia of the diaphragm, ulcers involving the lower esophagus and cardia, and adhesions.

The treatment, which is surgical, has been greatly improved since the advent of thoracic surgery.

**METASTASIS.**—F. L. Marting and B. Halpert (Yale J. Biol. and Med. 6: 541 (May) 1934) state that of 127 primary carcinomas in the gastrointestinal tract, metastases in the liver were encountered in 45 cases. Twenty were primary in the stomach, 4 in the bile ducts, 4 in the gall-bladder, 7 in the pancreas, 2 in the cecum, 3 in the sigmoid colon and 5 in the rectum. Of the 20 gastric carcinomas, 4 were located in the cardiac portion, 7 in the body, and 9 in the pyloric portion of the stomach. Metastases in the liver from the carcinomas primary in the cardiac portion and the body of the stomach occurred in the right lobe predominantly in 2, in the left lobe predominantly in 3, and in both lobes in 6 instances. From the carcinomas primary in the pyloric portion, metastases occurred in the right lobe only in 1 and in both lobes in 5 cases. The exact location of the metastases in the liver was not recorded in 2 instances and metastasis occurred by direct extension in 1 case.

**TREATMENT—Results of Resection**—P. Bull (Norsk mag f laegevidensk 95 1035 (Sept ) 1934) has analyzed 289 cases of cancer of the stomach, 206 in men and 83 in women, the fate of all but 5 being known. Radical operation was performed in 23.3 per cent. of the men and 30 per cent. of the women. In 20.2 per cent. of the cases in which operation could not be performed, clinical symptoms had been present for only 1 to 5 months. The author states that the patients with cancer of the stomach who undergo resection have an average life duration from 5 to 6 times longer than the patients in the other groups and he urges that in operation every effort be made to perform resection. The results of the operation depend fully as much on the degree of malignity of the cancer in each case as on its clinical duration. Tabulated review is given of the 11 patients still living from 3¼ to 13½ years after resection and of the 5 cases in which death occurred from recurrence after from 3½ to 9 years after resection.

**SPLEEN.—HEMATIC CYSTS.**—These cysts are classified by M. Mauro (Ann ital di chir 12 1547 (Dec 31) 1933) as follows: (1) acute, recently formed blood cysts, very similar symptomatically to complete rupture of the spleen; (2) subacute cysts in the process of organization, with repeated crises due to secondary hemorrhages, (3) chronic cysts organized and growing slowly and painlessly. He states that a healthy spleen normally located and not affected by altered vessels in the vicinity can be injured only by severe trauma, whereas a spleen in which the pulp has been previously altered by acute splenitis, passive congestion or premature atrophy, may be injured seriously by very slight trauma. Spontaneous ruptures outnumber those of truly traumatic origin. Mauro stresses the repetition of the initial syndrome in less severe form as crises of "colic," during one of which rupture may occur.

**Splenectomy** is always the operation of choice. According to statistics, the results of operations for well encapsulated cysts are good, whereas for traumatic rupture the mortality of splenectomy is high.

**GAUCHER'S DISEASE.**—Two cases are reported by E. B. Potter and C. C. McRae (Am. J. M. Sc. 185:92 (Jan) 1933), one of which improved immediately following **splenectomy**; the other patient had bone lesions mistaken for osteomyelitis and operation was done for this diagnosis. This patient was then given **liver extract** over a period of 11 months with occurrence of a remission characterized by symptomatic improvement, diminution in the size of the spleen and liver, and improvement in the blood picture. O. Ullrich (Ztsch f Kinderh 55.1, 1933) shows that in patients with Gaucher's disease splenectomy has its advantages and disadvantages. He reports a case in which splenectomy averted the acute danger to the child from severe anemia and hemorrhagic diathesis and improved the general condition. Soon after the operation, however, skeletal changes of a progressive, destructive character became manifest. The author concludes that since splenectomy does not influence the metabolic disturbance, which is the underlying cause of the disease, the diagnosis of Gaucher's disease does not justify the intervention.

**NECROSES OF SPLEEN.**—The necrosis is due to occlusion of the splenic arteries of small and medium size. Three types of flecked spleen are recognized, according to P. H. Guttman (Arch Path 17:187 (Feb) 1934): the arteriosclerotic, arteritic, and thrombotic. The *arteriosclerotic form* is the most common, comprising all but 3 of the 21 cases of flecked spleen reported in the literature. The arteriosclerotic form of flecked spleen is associated with renal lesions of hypertension, which in most cases produce death from uremia. The *thrombotic form*, described in a report of a case of eclampsia, is associated with multiple necroses of the kidney. The *arteritic type* is described in association with 2 cases of glomerulonephritis. Flecked spleen should be differentiated from multiple necroses of the Malpighian corpuscles associated with acute infectious diseases, as the pathologic changes and pathogenesis in the two conditions are dissimilar.

**SARCOMA OF SPLEEN.**—J. W. McNee (J Path and Bact 39:83 (July) 1934) states that this occurs in more than one histological type, i. e., the spindle-cell sarcoma, endothelial sarcoma and lymphosarcoma. The age and sex incidence are very variable, and apart from the splenomegaly and its accompanying signs and complications, only one clinical feature need be noted. A number of writers have pointed out that in sarcoma of the spleen the clinical picture may simulate fairly closely that of untreated pernicious (Addisonian) anemia, and may exhibit severe anemia, leukopenia, increased bile pigment in the blood, and even achlorhydria. In the case reported by Howard the knee and ankle jerks were absent and a remission occurred similar to those which were frequently seen in Addisonian anemia before the introduction of liver therapy.

**Metastases.**—The question of secondary metastatic growths in association with primary splenic disease is obviously important from its bearing on whether the condition is to be described as a true malignant growth or a reticulosis. It seems certain, however, from the available literature that metastases at a distance

are uncommon, although cases with many metastases have been described (Schneidewind, 1928).

**SPLENOCLEISIS.**—*Indications.*—The case of a child, 15 years of age, with a *severe anemia* associated with *splenomegaly*, is reported by B. Schiassi (Arch. ital. di chir. 36: 489, 1934), which he believed was secondary to thrombosis of the splenic vein. Splenectomy seemed to be the procedure of choice, but on account of the firm adhesions to the diaphragm, the poor general condition of the patient, and the marked enlargement of the spleen, the removal of which would entail the loss of a large quantity of blood, the author decided on splenocleisis, *i. e.*, extraperitoneal transplantation of the lower two-thirds of the spleen beneath the rectus muscle. Following this operation the patient's general condition improved, the spleen decreased in size and the erythrocytes increased to 4,500,000, the hemoglobin to 56 per cent., and the leukocytes to 3100. In order to reduce the cytolytic action of the reticuloendothelial cells of the spleen on the erythrocytes still further, **x-ray** irradiation was given over the transplanted spleen. Following this treatment, the blood picture improved.

**SPLENECTOMY.**—*Results.*—The late results of 27 splenectomies are reported by H. Tammann and K. Deutelmöser (Zentralbl. f. Chir. 61:492 (Mar. 3) 1934). Attention is called to the presence of Jolly bodies in the red cells after a splenectomy in otherwise healthy persons. The best results, approximating a permanent cure, were obtained in *hemolytic icterus* and next in order were *Gaucher's disease* and *essential thrombopenia*, in which the main clinical symptoms were absent years after the splenectomy was done. The same can be said of *splenic tumors* resulting from hepatosplenic disease (Banti). The question of splenectomy for splenic tumors of leukemic origin presents itself only in exceptional cases, while its removal in pernicious anemia has been generally abandoned.

**WANDERING SPLEEN.**—From the literature, I. Abell (Ann. Surg. 98: 722 (Oct.) 1933) has collected 95 cases of wandering spleen with torsion of the pedicle. To these he adds 2 personal cases. The fact that 14.3 per cent. of the patients were under 20 years of age supports the theory that a congenital elongation of the splenic pedicle is essential for the occurrence of the condition. The fact that only 19 per cent. of the subjects were over 40 years of age suggests that relaxation of the abdominal wall and the ligaments which support the abdominal viscera is not a cause of major importance. Pregnancy did not seem to be a factor of special significance. Primary **splenectomy** was performed in 83 cases. Detorsion and replacement were done occasionally, but the author advises against them.

**SUBPHRENIC ABSCESS.**—A. Ochsner and A. M. Graves (Ann. Surg. 98: 961 (Dec.) 1933) have studied 3322 cases of subphrenic abscess collected from the literature in addition to 50 personal cases.

Subphrenic abscesses occur much more frequently than is generally supposed, but as most of these infections subside spontaneously, the incidence of subphrenic infection without abscess formation is much higher than that with abscess formation. Subphrenic abscesses occur 3 times more frequently in males

than in females. In the authors' series of cases no racial predisposition to such abscesses was apparent. Thirty-two per cent. of the patients were in the fourth decade of life, and 70 per cent. between the ages of 9 and 40 years.

**Etiology.**—Subphrenic abscess usually follows an intraperitoneal suppurative process. The most frequent antecedent conditions are perforated appendicitis and perforated lesions of the stomach and duodenum. Of the total number of cases reviewed, appendicitis and perforated lesions of the stomach and duodenum were the original focus in 59 and 54 per cent., respectively. The incidence of subphrenic abscess complicating acute inflammation of the appendix varies in collected series of cases from 0.34 to 6.1 per cent. The average incidence in 11,017 cases of acute appendicitis was 1.1 per cent. The incidence is undoubtedly higher than these figures indicate because in many cases a subdiaphragmatic complication is not suspected. In the authors' series of cases in which positive cultures were obtained from the subphrenic space, colon bacilli were present in 40 per cent., streptococci in 40 per cent., and staphylococci in 20 per cent. The most frequent site of the abscess is the right posterosuperior space. This space was involved in 28.8 per cent. of the collected series of cases and in 60 per cent. of the authors' cases.

**Diagnosis.**—The clinical picture of subphrenic abscess is generally one of continued infection following an intraabdominal suppurative process. Of the cases reported by the authors, the onset was sudden in 16 per cent. and insidious in 14 per cent. In 70 per cent., systemic manifestations continued following drainage of the original suppurative process. In addition to the systemic manifestations of infection, there were localizing signs such as a sense of pressure in the upper abdomen or loin and difficulty in breathing, especially on deep inspiration. Persistent tenderness over the right twelfth rib or along the right costal margin in such cases is indicative of subphrenic infection. Limitation of respiratory movement, together with elevation of the diaphragm, occurs early. Diagnostic aspiration is contraindicated because of the danger of contaminating uninvolved portions of serous cavities. Intrapleural complications are usually due to delay of diagnosis and treatment of subphrenic infection.

**Treatment.**—In all cases of subphrenic infection in which suppuration has not occurred **conservative treatment** is indicated. When *suppuration* has developed, **incision** and **drainage** should be done with care to prevent contamination of an uninvolved cavity. In 1072 reported cases of subphrenic abscess in which nonoperative treatment was given, the mortality was 91.1 per cent., whereas in 1693 cases in which drainage was established, it was 33.6 per cent. In the collected series of 189 cases of subphrenic abscess drained without contamination of the pleural or peritoneal cavities, the mortality was 21 per cent., whereas in 305 cases in which transpleural drainage was established, it was 39 per cent. and in 337 cases with transperitoneal drainage it was 35.5 per cent. In the authors' series, the mortality following extraperitoneal, transpleural, and transperitoneal drainage was 13.6, 50, and 41.6 per cent., respectively.

The *technic* of *Ochsner and Graves* of the "**retroperitoneal operation**" is in part as follows:

Under paravertebral block analgesia an incision is made over and parallel to the twelfth rib. The entire twelfth rib is resected subperiosteally. The erector spinæ mass of muscles is retracted medially and a transverse incision is made at right angles to the spine across the bed of the resected rib at the level of the spinous process of the first lumbar vertebra. This incision passes through the bed of the twelfth rib and the attachment of the diaphragm. After the diaphragm has been incised, the renal fascia is encountered. This is continuous above and anteriorly with the posterior parietal peritoneum. The kidney is displaced downward by means of the index finger and the infrahepatic space is palpated.

In those cases in which an abscess of the right posterior superior space is suspected, the peritoneum on the undersurface of the diaphragm can be separated from the diaphragm by means of the finger. This separation may be carried upward as far as the dome of the liver and should be extended until the abscess is reached. By means of the mobilizing finger, the abscess cavity is opened by plunging the finger through the abscess wall, which is adherent to the mobilized parietal peritoneum. Large, soft, fenestrated rubber tubes are introduced into the abscess cavity and brought out through the wound. Through this incision, adequate evacuation of abscesses located in the right posterior superior, right extraperitoneal, right inferior, and even occasionally right anterior superior spaces, may be accomplished without traversing or contaminating either the pleural or peritoneal cavities.

Abscesses located in the right anterior superior, right inferior, left anterior inferior and left superior spaces can be drained extraperitoneally through the anterior abdominal wall. Abscesses of the right inferior space can be drained by the retroperitoneal approach. In those cases in which there are abscesses above the liver, the suppurative process can be approached and drained extraperitoneally without contamination of uninvolved pleura or peritoneum by employing an approach suggested by Clairmont.

The authors exemplify the technic of the retroperitoneal operation by the low mortality rate (97 per cent) obtained following its use in 31 cases in which they operated.

They give the mortality rates in the personal and collected cases and state that in order to decrease the mortality, it is necessary to avoid contamination of uninvolved portions of the pleura and peritoneum during drainage. This may best be accomplished by **draining the abscess extraperitoneally.**



# Orthopedics

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**DISLOCATIONS.—HIP.—*Congenital Dislocation.***—Subsequent changes in the congenitally dislocated hip reduced by the Paci-Lorenz method are discussed by E. H. Lagomarsino (Rev. ortop. y traumatol. 3: 359 (Apr.) 1934). These changes depend upon: (1) the time at which the reduction is done; (2) correct centering of the cephalic ossifying nucleus until there is perfect retention by reconstruction of the acetabular roof; (3) the gentleness and smoothness of manipulation during reduction and subsequent handling; (4) the reconstructive power of the reduced hip; and (5) the extent of osteochondral changes instituted by the reduction. To a certain degree the last two factors are governed by the first three. There are no infallible signs upon which an accurate prognosis can be based.

The reduced hip frequently presents changes of enchondral ossification, especially in the epiphyseal nucleus. A study of this ossifying center shows 2 principal groups of changes. In the first group are the decalcifications and simple changes of enchondral ossification of an osteoporotic type. These changes are the "white nuclei" with a pale appearance in the x-ray film. Decalcifications may occur diffusely throughout the nucleus or in only a part of it. They may be central or peripheral. They often produce a "moth-eaten" appearance and have been interpreted as indicating enchondritis or osteo-arthritis.

The second group of changes are those of the center of ossification in the head of the femur which produce increased density and constitute the "dark nuclei." They are indicative of severe nutritional changes. They first appear as a massive and regular nuclear condensation without changes in form. The density is due to an increase in the content of opaque salts. The condition is regarded as a traumatic osteochondritis. Successive views demonstrate the gradual formation of spongy bone.

The etiopathology of the osteochondritis occurring in the congenitally dislocated hip after its reduction is difficult to explain. The most satisfactory theory attributes the condition to trauma. The prognosis is much better when immobilization is prolonged and the bearing of body-weight is avoided throughout the period of repair, which is usually from 12 to 18 months.

**TEMPOROMAXILLARY JOINT.—*Habitual dislocation,*** without fixation of the jaw, of the temporomaxillary joint, according to P. Friez (Presse méd. 41: 1916 (Nov. 25) 1933), occurs most frequently in young individuals, particularly girls. It is probably due fundamentally to laxity of the ligaments and the joint capsule and possibly also to intraarticular malformations. Particularly after traumatism, it may be accompanied by crepitations and pain. The condyles may become dislocated on one or both sides, but are returned to the glenoid fossæ without difficulty.

As the condition is relatively benign, the *treatment* should be simple, consisting of such measures as the wearing of an **elastic support** for a considerable period of time or **intramuscular injections of alcohol**.

L. Mayer describes an **operation** (J. Bone and Joint Surg. 15: 889 (Oct.) 1933) for the cure of intractable slipping of the temporomandibular joint. It consists in the formation of a bone block just anterior to the eminentia articularis.

of the temporal bone to prevent forward sliding of the condylar process of the mandible.

The *symptoms* of true intraarticular disturbance of the jaw joint usually consists of a snapping sensation, pain, and locking of the joint. These are due either to a true dislocation or an internal derangement, usually associated with abnormality of the interarticular fibrocartilage. In the latter type there is abnormal laxity of the cartilage. This may be cured by removal of the meniscus, just as is done in the knee joint. One such case is reported.

In cases of true dislocation of the jaw there is shallowness of the temporal fossa, which allows the condyle to rise forward from it over the eminentia articularis. The author's **operation** is carried out under local anesthesia. The posterior portion of the zygomatic process over the affected joint is exposed by a horizontal incision which is extended posteriorly over the pinna of the ear. One inch of the process is resected, care being taken to prevent injury of the branches of the facial nerve. The capsule of the joint is opened and the movements of the sliding condyle and cartilage are observed as the patient opens his mouth. The cartilage is usually removed and the resected bone used as a graft by inserting it into a vertical groove cut in the temporal bone just anterior to the eminentia articularis. The effect of the bone block is then studied as the patient again opens his mouth. The capsule is closed carefully. On completion of the operation, a plaster helmet entirely encasing the head is applied for from 4 to 6 weeks.

E. W. H. Groves in *recurrent* dislocations of the jaw (Ann Surg 100 20 (July) 1934) uses the tendon of either the palmaris longus or the brachioradialis, passes it around the neck of the jaw and then through a hole drilled in the mastoid process from behind, inward and forward, pulls it tight and sutures the two ends.

**CARPUS.—Diagnosis.**—In carpal lesions, P. Saucier Toledo (Cir. ortop. y traumatol. 1 217 (Oct.) 1933) states that a clinical diagnosis is difficult and x-ray examination of both wrists is indispensable. Anteroposterior and lateral x-ray pictures should be taken.

Fracture of the *scaphoid* is characterized by symptoms of sprain of the wrist with the maximal manifestations in the anatomical snuff-box. In old cases it is suggested only by an increase in the thickness of the external carpal column. The fracture usually occurs in the medial part of the bone. Displacement of the fragments is absent or slight.

*Subtotal dislocation* of the carpal bones is frequent. The condition must be differentiated from bipartite scaphoid. The fracture must be reduced, if possible, and the wrist immobilized for 6 weeks between flexion and extension. If reduction is impossible, the fragments must be extirpated.

*Subtotal retrolunar dislocation* of the carpus is characterized by displacement of the os magnum behind the semilunar bone. The dorsal dislocation may occur with or without enucleation of the semilunar bone, depending on whether the anterior radiolunar ligament tears or not. The enucleated semilunar bone frequently rotates 90° around the anterior radiolunar ligament as an axis. Pain and loss of function are marked, the wrist becomes round, and symptoms of nerve

compression often develop. At the base of the third metacarpal the normal depression is obliterated by the head of the os magnum.

**Treatment.**—It was not until Böhler, H. Pich and M. Bracher (Chirurg. 5:786 (Oct 15) 1933) proposed a new procedure, making use of his screw apparatus, that it became possible to bring the semilunar bone back into its original position by conservative measures. Konjetzny proceeded in a similar manner, but opened the carpus from the dorsal side. He, too, obtained a good result. However, there is a time limit even to these methods. If more than 6 months have passed since the accident, the articular surfaces have become changed by inflammatory deposits so that the semilunar bone no longer fits into its original bed and the ligaments have shrunk extensively. Under such conditions, extirpation of the bone is necessary. Bohler is willing to remove the semilunar bone only when there is a disturbance of the median nerve. In the absence of such a disturbance, he regards the operation superfluous. The authors do not agree with Bohler on this point. In operating on an old dislocation of the semilunar bone which had undergone torsion to 90°, they found the semilunar bone wedged firmly between the other bones. The superficial flexor tendon was shredded in this region, and only from 1 to 2 mm. thick. Extirpation of the semilunar bone brought about great improvement in the symptoms. This case shows that, in addition to the well-known disturbances of the median nerve in old dislocations of the semilunar bone, there may be injuries to the flexor tendons which may easily have serious consequences, since at first it causes only vague symptoms that cannot be distinguished from the symptoms of the dislocation of the semilunar bone. If a wearing through or tearing of the tendon has already occurred, it is too late for surgical intervention. The authors, therefore, recommend extirpation of the semilunar bone in every case of dislocation in which reposition is impossible.

Operation for *late reduction* is described by E. D. McBride (South. M. J. 26:672 (Aug.) 1933). The author believes that the success of the operation for late reduction depends on complete freedom of the ligamentous contraction and fibrous tissue attachments of the anterior horn to the radius, the complete removal of fibrous tissue in the cavity formerly occupied by the semilunar bone, and of abnormal attachments of the os magnum, and the security of the semilunar bone in its normal articular bed, so that it cannot slip or rotate forward.

**Technic.**—In performing the operation, an incision about 1½ inches long is made on the dorsum of the wrist, immediately to the ulnar side of the extensor carpi radialis. The vein and nerve, together with the extensor indicis tendon, are retracted to the ulnar side and the extensor carpi radialis to the radius side. The fibrous tissue in the bed formerly occupied by the semilunar bone is excavated and a smooth curved periosteal elevator is passed forward to free the anterior horn contraction from the radius. The bone, which lies in a plane entirely anterior to the carpal bones, is then pried into position by a Davis skid or a similar instrument. If it cannot be reduced without too much trauma, it is better to make an interior incision immediately to the ulnar side of the palmaris longus, with its center over the radio-carpal articulation. The group of flexor profundus tendons is retracted to the ulnar side and the median nerve and palmaris longus tendon are retracted to the radial side. Complete reduction may be recognized by the contour of the dorsal horn. If the bone has a tendency to pull forward or is not entirely in alignment with the transverse plane of the wrist, the

anterior ligament is not entirely free, in which case a crevice is made in the anterior face of the dorsal horn of the semilunar bone with a curet, creating a hook into which a strand of number 00 catgut is inserted and sutured to the dorsum of the radius. The semilunar bone is thus checked in full dorsiflexion to the radius.

**FRACTURES.**—*Introduction.*—At the symposium on fractures at the American Academy of Surgeons, C. L. Scudder (Surg Gynec. and Obst. 58 474 (Feb 20) 1934) outlined the organization of the Committee on Fractures

There are 29 regional committees composed of 300 volunteer members whose interest lies in hospital standardization, courses, teaching, and development of material. The greatest single need in the fracture field is more trained men.

F. N. Bancroft (*Ibid*, p 476) reports the aims of education of the Fracture Committee as (1) Greater stress be placed on pathology, process of repair and fundamentals of fractures while in school; (2) special and separate fracture services in each hospital with instruction for internes; (3) postgraduate courses. Fractures as a rule are poorly taught

R. H. Kennedy (*Ibid.*, p 479) advocates the teaching of responsible lay persons, such as boy-scouts, firemen, policemen, etc., and the early transportation of cases of fractures of the long bones by traction methods, thus lessening the chance of compounding them

I. Cohn (*Ibid*, p 485) emphasizes that x-rays cannot always diagnose a fracture, and the surgeon should depend upon his clinical impression

A. Stendler (*Ibid*, p 487) outlines fracture disabilities of the wrist as due to (1) disalignment impairing range of motion; (2) degenerative arthritis; (3) progressive contractures, (4) secondary involvement of median and ulnar; (5) Sudeck's atrophy

**Pathology.**—O. Goetze and W. Brackertz (Arch f klin. Chr 178 565 (Dec 21) 1933) demonstrated histologically in animal experiments that the mere operative act of exposing the fracture, without an attempt at reduction and fixation, regularly interfered with the process of normal consolidation. The rapid metaplasia of the early fibroblastic tissue in temporary osteoid and chondroid callus is much delayed. The wound developed an increased acidity. These disturbances in consolidation are increased by injury to the periosteum. Postponement of the time of operation to a later date, when sufficient temporary callus is present, diminishes the disturbance in metaplasia. The author demonstrated in histologic studies that the ends of the fragments in every fracture undergo a necrosis and a breaking down of the bony structures.

The histologic studies of the closed healing and operative healing of fractures furnish a basis for preference in favor of the conservative methods. These can act as guides when the advantages of exact anatomic reduction require osteosynthesis. The operative procedure should be limited to a few essentials. Exposure should be avoided, or, if necessary, the operator should be content with the least exposure. Further injury to the periosteum, periosteal callus and periosteal blood-vessels should be avoided. It is preferable not to leave a foreign body in the wound and, if advisable, only the smallest foreign body susceptible of being removed through a small incision.

**Complications.**—NONUNION.—R. W. Jones (Brit. M. J. 1:936 (May 26) 1934) states that nonunion of fractures is almost always avoidable and is a complication entirely within the control of the surgeon. Many physiologic and biochemical factors may be concerned in the rate of union of fractures, but the only factor that is of practical importance in determining nonunion is inadequate immobilization. Immobilization may be inadequate in that the fracture is allowed movement within the splints or plaster; rotatory movement is especially inimical to union; and immobilization is not continued for a sufficiently long period. There can be no fixed period of immobilization for any fracture; the average duration of immobility may be exceeded in occasional cases by many months. Hyperemic decalcification and ischemic recalcification of bone must be accepted as pathologic facts.

The initial traumatic hyperemia mobilizes calcium salts from the bone ends, but rapidly subsides and allows recalcification of the young connective tissue to form callus. With final repair and fibrosis, the callus consolidates by increased calcification. If the hyperemia is perpetuated by the trauma of movement, there is excessive decalcification—a crack fracture becomes a gap fracture. This is the *first stage* of nonunion. In the final phase of ischemic fibrosis the surfaces of the fragments undergo sclerosis; this is the *second stage* of nonunion.

The two stages of nonunion are distinguishable by the x-rays. The first stage is cured by immobilization. In the second, preliminary revascularization is necessary by a drilling or grafting operation. The infected compound fracture is pathologically similar to a simple fracture, except that the initial stage of decalcification is prolonged. If it is immobilized, the fracture will usually unite. An old infected fracture that has not been immobilized is in the first stage of nonunion so long as the infection is active, but passes into the second stage of nonunion after quiescence of the infection. In the *first stage*, **sequestrectomy** without "scraping," followed by **immobilization**, determines union. In the *second stage*, a **revascularizing operation** is necessary. Even if the operation is followed by a flare of infection, the fracture still unites if it is immobilized.

**Treatment.**—HEALING OF FRACTURES.—A great many factors and their relation to fracture healing are being experimentally studied. K. O. Haldeman and J. M. Moore (Arch Surg 29:385 (Sept) 1934) report failure of local excesses of monocalcium, tricalcium and dicalcium phosphate and calcium glycerophosphate. None of the calcium and phosphorus compounds used in excess seemed capable of accelerating the normal rate of healing. In this respect the results fail to follow the well-recognized chemical law that increasing the concentration of the reacting substances speeds up the reaction. Because of this fact it is probable that the process of ossification is more than the purely chemical equation which certain authors describe.

G. Bankoff (Arch f klin Chir 179:256 (Mar 15) 1934) believes that the **sexual hormones** have a direct effect on the blood picture and hence on fracture healing. Experiments on castrated animals are cited. He advocates local injection of sexual hormones on the tenth day after operation for pseudoarthroses.

The effects of **irradiated ergosterol** on the consolidation of fractures in experimental animals have been variable. J. Morelle (Rev belge sc méd 5:481

(Aug-Sept.) 1933) states that the original observations of Pfannenstiel (1927) have been widely confirmed. When animals are given excessive doses of irradiated ergosterol, they develop diarrhea, which leads to death within 10 to 40 days and necropsy discloses extensive calcification, chiefly of the arterial system, the myocardium, the kidneys, and the stomach.

The intoxication is favored by a diet rich in calcium. Very different effects are produced by a diet poor in calcium. Toxic symptoms appear late, degenerative lesions and calcification are slight or absent, and there is a marked osteoporosis. The calcium-phosphorus ratio in the diet is important, deviations from the normal in either direction being harmful. When the quantity of calcium is optimal and that of phosphorus excessive, the latitude between the therapeutic and toxic doses becomes reduced.

Adult animals are more sensitive to excessive amounts of vitamin D than young animals. The dog is an exception. Rachitic animals tolerate larger doses than normal animals.

Thymectomy decreases, and splenectomy increases, the toxicity of vitamin D.

The *dose* of irradiated ergosterol which will cause toxic symptoms is between 5000 and 10,000 antirachitic units.

The *hypercalcemia* following the administration of vitamin D is either exogenous or endogenous, depending upon the quantity of calcium in the diet. When the calcium intake is low, the calcium balance becomes negative and there is rarefaction of the skeleton. Under these conditions the intestinal excretion of calcium is reduced and its excretion in the urine is increased. The changes in the metabolism of phosphorus roughly parallel those of the metabolism of calcium.

The *changes in the bones* consist essentially of decalcification and hypercalcification. One may succeed the other. Decalcification affects principally the ribs, where it produces a picture somewhat resembling that of experimentally produced rickets. There is resorption in the metaphysis which may lead to fracture. In this change the osteoclasts play a minor rôle. Enchondral osteogenesis is arrested, and there is an intense hyperemia of the marrow. When these changes have been produced, the excess of vitamin D has usually been combined with a diet low in calcium.

Young animals given moderately large doses of ergosterol show increased density of the bones, calcification of the growth cartilage, and direct metaplasia of the cartilage into bone. The latter two changes lead to arrest of growth.

It appears that up to a certain dose, irradiated ergosterol produces increased density of the skeleton. When the dose is exceeded, rarefaction occurs. The two processes may evolve simultaneously both in the bones and the teeth, these tissues acquiring an alveolar appearance.

In view of these facts, Morelle's (*Ibid*) experiments were planned to study the *effects of varying doses* of irradiated ergosterol on the repair of fractures. The experimental animals were rats and rabbits. Fractures were produced in either the bones of the hind foot or the fibula, and the development of the callus was studied by the x-rays and histologically.

In young rats, doses of 1000 antirachitic units hastened the formation of the callus, while doses of from 20,000 to 40,000 daily delayed it.

In adult rats a retarding action on callus formation was noted whenever the dose of ergosterol reached from 7500 to 10,000 units. When fewer than 1000 were given, callus formation was stimulated.

Histological examination on the twenty-first day after the fracture showed that the development of the osseous callus in the control rats was well advanced but less advanced than in the rats receiving small amounts of vitamin D. The rats receiving massive doses of vitamin D showed only fibrous calluses. The difference between the control animals and those receiving large doses of vitamin D were noticeable as late as the fifty-fourth day.

Examination of the blood revealed that 1000 units of vitamin D were about as effective in raising the blood calcium as massive doses.

In the study of the favorable effect of vitamin D on the consolidation of the fractures, it was found that the optimal dose was between 50 and 1000 units. The action of the vitamin was operative between the fourteenth and twenty-eighth days. During this period the callus was chiefly cartilaginous and it appeared that the action of vitamin D was exerted chiefly in cartilage. This observation is in agreement with the mechanism of cure in experimental rickets.

The unfavorable effect of an excessive dose of vitamin D on the callus appeared later in young animals than in adults. In both, the cause was the generalized demineralization of the skeleton.

TREATMENT OF SPECIAL FRACTURES—*Superior Extremity*—R. Anderson (J Bone and Joint Surg 16 379 (Apr) 1934) has developed a **mechanical robot** for the **reduction** of fractures of the *radius* and *ulna*. By the use of pins, one through the upper end of the ulna and one, a half-pin, through the lower end of the radius, and a miniature fracture table or tablette, traction can be made on the fragments and correct alignment obtained and held while the cast incorporating the pins is applied from axilla to knuckles. The half-pin is equipped with 2 square flanges to gauge its penetration into the radius, to insure anatomical rotation when it is placed against the horseshoe of the traction apparatus, and to prevent rotation of the pin in the plaster. Sidewise slipping of the radius on the pin is prevented by a U-shaped aluminum cuff slipped over the forearm from the ulnar side.

The author states that this device is applicable to compound fractures and, with a third wire, to complicating fractures of olecranon and lower humerus.

N. J. Howard and L. Eloesser (*Ibid* 16 1 (Jan) 1934) point out that in fractures of the *upper end of the humerus*, control of the short fragment is obtained by virtue of the long head of the biceps bridging the fragments and the remaining untorn periosteum. Clinical experience indicates that when the arm is abducted, the pull of the abductor muscles makes approximation difficult to obtain and still more difficult to preserve. Accurate approximation may be obtained and maintained by downward traction, a fact demonstrated on the phantom model and by clinical experience. The integrity of the long head of the biceps tendon is necessary for the use of this method. Reduction under **local**



**anesthesia** for fractures of the upper end of the humerus may be accomplished by the following maneuver:

With the patient sitting upright, supporting the injured arm across the body with the opposite hand, a folded face towel is placed over the forearm just below the elbow. A 4- or 6-inch heavy muslin bandage is looped over the towel and tied in a sling, so that its lower end hangs from 8 to 12 inches from the floor. An assistant grasps the wrist of the injured arm and, bringing the forearm at right angles to the body in the sagittal plane, maintains right-angled flexion of the elbow. The surgeon then places one foot in the sling, grasps the upper arm with both hands below the line of fracture, and slowly and steadily increases the amount of pressure on this foot. The two hands grasping the arm below the fracture are used to force the upper end of the distal fragment laterally, anteriorly or posteriorly, as required by the displacement. For the dressing, a small pad is placed in the axilla and along the arm. The forearm is held flexed by a sling, while the arm is loosely bound to the body, the elbow is left free to allow the weight of the arm to act as a traction force.

A very similar method has been advocated by Frankan, who believes that in fractures of the *surgical neck*, reduction is effected under anesthesia most easily and simply by exerting strong traction in the line of the long axis of the arm for several minutes and then adducting the arm across the trunk while continuing the traction. This procedure permits accurate reposition of the fragments.



Fig. 1—Diagrams of left humerus. XY is line of fracture in upper fragment and AB the line of fracture in lower fragment. (a) shows fracture unreduced, (b) effect of simple traction in line of limb, (c) effect of adduction bringing points X and A into apposition, (d) final result.

After the reduction, the arm should be immobilized for 1 week, and at the end of that time active movements permitted gradually. Complete restoration of function is generally obtained in 6 weeks.

Fractures of the *carpal scaphoid* when seen early require absolute immobilization in well-fitting **casts**, according to W. Kuchel (Munchen med Wchnschr 80:1350 (Sept. 1) 1933), J. H. Burnett (New England J Med 211:56 (July 12) 1934) and G. Murray (Brit J Surg 22:63 (July) 1934), for 6 to 8 weeks. Cases that have undergone malunion should have accurately shaped **bone grafts**, rather than excision as formerly practiced.

**Spine**—The majority of continental opinion is against reduction of compression fractures of the vertebræ, preferring functional treatment, according to V. Gorinevskaya and T. F. Dreving (Sovet. khir. 5:13 (No. 4) 1933). L. Bohler sides with the English and American views, though these were opposed by all discussers at the last meeting of the Congress of German Surgeons (Arch f klin Chir. 177:424 (Oct. 18) 1933). Since 1930 the author began to treat his patients, after the **reduction** of fracture and fixation in a **plaster jacket**,

by putting them through **systematic exercises**. Disability after a vertebral fracture, when injury to the cord and injury from subluxation are discarded, is in a direct relation to the degree of distortion of the vertebral column. Vertebral fractures accompanied by distortion of the vertebral axis lead to permanent disability because the static conditions are changed and because still further distortion of the column will cause displacement of the thoracic and abdominal viscera. No injury to the spinal cord will take place if the reduction is accomplished with the aid of local anesthesia, the extension in suspension taking from 15 to 25 minutes until the gibbosity disappears and a marked lordosis becomes evident. Also A. G. Davis (J. Bone and Joint Surg. 11:133 (Jan.) 1929); R. W. Jones (*Ibid.* 16 30 (Jan.) 1934).

In the presence of paralytic symptoms, the surgeon is certainly obliged to reduce the fracture. **Laminectomy** becomes necessary in a few cases in which reduction cannot be accomplished by extension. This is the case when the articular processes are dislocated but not fractured. When a patient is put in bed in a plaster cast, he is rendered both physically and psychically ill. The muscles become weak, the bones lose some of their calcium content, and the vertebral joints become stiff. The author's patients are permitted to **walk without a cane** on the second or third day after the application of the cast. Twice daily the patients are put through **exercises** of the arms, bending the knees, extension of the legs and muscling up the body on rings. To strengthen the muscles of the back, the body is made to rise from a horizontal to a vertical position. Lifting the thighs while lying flat on the back develops particularly the ileopsoas muscle, which bears the closest relation to the fractured vertebræ. Toward the end of the treatment the patients are made to carry a weight on their heads for from 20 to 40 minutes. They begin with a weight of from 1 to 2 kg ( $2\frac{1}{2}$  to  $4\frac{2}{5}$  lbs), which is increased to 50 kg. (110 lbs). Patients treated in this manner are in the best physical and mental condition.

*Inferior Extremity*—Intracapsular fracture of the *femoral neck* is the ground for the most rabid controversy at the present time in orthopedics. Royal Whitman (Am J Surg 21 335 (Sept) 1933) says that, according to statistics from a variety of sources, union of medial fracture of the femur occurs in approximately 65 per cent of cases treated by his **abduction** method. For cases in which faulty treatment has been employed, he recommends **open operation**, and for those showing incapacity for repair he suggests the **Whitman reconstruction operation**. The latter consists in removal of the distorted head, molding the remaining portion of the neck, and transplantation of the trochanter with its attached muscles down the shaft.

Methods of spiking the fragments, such as the use of the flanged nail by Smith-Petersen, are rejected by Whitman, as he believes that recovery depends on reconstruction of the bony structure and this will be retarded by the injury to the cancellous tissue caused by the introduction of a nail. He is of the opinion that many months are required for the repair of a medial fracture, and doubts whether any form of operative intervention will greatly shorten the period of disability.

He states that the abduction method relieves the pain, permits change of posture, and has not only greatly extended the range of the positive treatment of fractures, but has materially reduced the death rate.

A. W. George and R. D. Leonard (Am J. Roentgenol 31:433 (Apr.) 1934) have developed a **curved cassette** so that vertical films of the femoral neck may be obtained. He attributes the high percentage of unsatisfactory results to inaccurate reduction rather than inadequate blood supply to the head fragment. Vertical views aid in determining the condition of the femoral neck which antero-posterior films would suggest "absorption."

Some means of internal fixation is rapidly gaining favor as immediate or early treatment in this type of fracture. Smith-Peterson, designer of a 3-flange nail, is the leading crusader. He early advocated **open reduction and nailing**. This method is necessarily limited to a few, experienced in hip surgery. H. H. Wescott (J Bone and Joint Surg. 16:372 (Apr) 1934) has simplified the procedure by determining the angle of the femoral neck from the opposite side, obtaining a closed reduction, and then nailing through a small incision over the great trochanter.

Wescott's procedure in cases of transcervical fracture of the femur is to immediately apply **Buck's extension**. He states that in cases of transcervical fracture of the femur, immediately on admission to the hospital, a Buck's extension is applied to prevent muscle spasm and overriding of fragments and to lessen shock. The forward angle, or angle of antroversion, is determined by means of a portable x-ray machine. The exact length of the nail necessary to fix the fragments is ascertained. The point of the blade must penetrate the proximal fragment deep enough to give stability without encroaching on the cartilage. The head of the nail should extend  $\frac{1}{4}$  inch beyond the cortex to facilitate the extraction of the nail at a later date. From 24 to 48 hours later, without releasing the pull of the Buck's extension, the patient is removed to the operating room. A flat Bucky diaphragm or tunnel is placed under the fractured hip and the x-ray tube is centered over the hip. Under an anesthetic, the Buck's extension is removed and the fracture reduced by internal rotation and gentle flexion of the femur at the hip. This manipulation is repeated 2 or 3 times. During flexion, sufficient traction is made to counterbalance the weight of the thigh. The leg is extended in internal rotation. Stereoscopic x-ray pictures are made to prove reduction.

If reduction is complete, an incision from  $2\frac{1}{2}$  to 3 inches long is made over and below the trochanter. One-half inch below the vastus muscle, a small hole is bored into the bone and narrow slits are made with an osteotome to receive the blades of the nail. The roentgenogram protractor is placed over the x-ray picture taken after reduction, with its base along the shaft,  $\frac{1}{2}$  inch below the vastus muscle, and the lever is made to correspond with the center of the neck of the femur. The reading of the number of degrees of angulation of the neck with the shaft is made and the bone protractor is set at a like angle and clamped. The nail is driven into the flattened neck of the femur at the angle indicated by the lever of the bone protractor. The fracture is impacted and the wound is closed. Stereoscopic x-ray pictures may be made, if desired, to check the course of the nail.

The author used this procedure in 12 cases, irrespective of age or general condition. In spite of the fact that several of the patients were poor surgical risks, there were no deaths that could be attributed to the operation or its after-effects.

R. Anderson (Surg. Gynec. and Obst. 58:639 (Mar) 1934) and R. A. Griswold (*Ibid* 58:900 (May) 1934) have independently described **robots** for the reduction of fractures of both bones of the *leg*. Both robots are modifications

of the Leroy Abbott bone lengthening apparatus. Steinman pins are controllable by the robot so that anatomical alignment and end-to-end apposition may be obtained and checked by x-ray without danger of losing position. If the position is satisfactory, the pins are incorporated in a cast and, after drying the robot, removed. Details of Anderson's technic are as follows:

The preparation of the leg includes shaving and cleansing with soap and water, sterilization with ether and iodine, followed by alcohol if the iodine is strong. An injection of from 5 to 20 c.c. ( $1\frac{1}{4}$  to 5 drams) of a 2 per cent. solution of **procaine hydrochloride** is made into the skin and down into the periosteum on each side of the tibia at both sites of transfixion, while from 20 to 60 c.c. ( $\frac{2}{3}$  to 2 ounces) is injected into the hematoma and round the end of each fragment. The distal pin is put in straight through the center of the tibia at a point 2 fingerbreadths superior to the tip of the internal malleolus. Recently, the author has changed the site of the superior insertion to transfix the condyles of the tibia at their widest part midway between the anterior and posterior surfaces, just distal to the knee joint. Without incising the skin or preliminary drilling of the bone, each stainless steel Steinmann pin is forced through by a rotary hand pressure alone. Sterile dry dressings, about 2 inches square, spiked over each pin end, safeguard infection; they are held close to the wound by a bandage of nonsterile sheet wadding. By grasping the foot and pulling on it, the assistant raises the leg while the splint is placed beneath and the pins are clamped to their respective horseshoes. The foot and ankle are padded with sheet wadding, special attention being given to the protection of the heel. All malposition is now controllable; traction and rotation are adjusted, angulation is corrected and the adjustable foot rest is set. When the reduction is complete, it is roentgenographically checked. Separation of fragments, due to overtraction, must be assiduously avoided because, notwithstanding perfect alignment, usually no result can be considered satisfactory without end-to-end pressure contact.

Immobilization of satisfactory reduction is completed by the application of a cast, which firmly incorporates the pins and generally extends from midhigh downward over the foot plate to slightly beyond the toes. The sole of the foot should be reinforced with a 4-inch plaster bandage. When the plaster is set, the pin clamps are loosened and the leg in its cast is lifted free from the horseshoes and from the foot plate. Ordinary corks are placed on the ends of the pins, which are then covered and fastened to the cast by a plaster bandage. A window cut over the patella serves for subsequent mobilization of the cap, allowing freedom of movement.

*Jaw*.—N. Stromberg (*Acta chir Scandinav* 74: 379, 1934) states that fractures of the collum and capitulum mandibulæ are undoubtedly much more common than has been heretofore believed.

Luxation fractures are of special interest from the surgical point of view. The lesions are typical and nearly always require surgical treatment for a satisfactory result.

At the General Hospital and Sahlgren Hospital, Gothenburg, 5 cases of luxation fracture were under treatment in the course of the past year. In one of these the fracture was bilateral. In 4 there was a definite change in the bite. In the latter, the treatment consisted of **extirpation of the articulated head**. For the operation an incision behind the ear is best, as when such an incision is used a good view of the operative area is obtained, lesions of the facial nerve are avoided, and the scar is cosmetically satisfactory.

In 3 cases reviewed the jaws were fixed after the operation by an intra-maxillary connection. In 1 case a normal position between the teeth of the upper and lower jaw was obtained without such fixation. In all the cases the after-

examination proved the results to be satisfactory. In the case in which there was no change in the bite, operation was not considered indicated.

When there is a change in the bite, operation should be undertaken as soon as the patient's condition permits, for if the jaw is allowed to remain for long in a position in which coaptation of the teeth is inexact, reduction and retention are rendered more difficult by muscular contraction and the accumulation of callus, the course of recovery is prolonged, and the ultimate result is more uncertain.

**FRACTURES IN CHILDREN.**—Epiphyseal separation of the long bones is reviewed by E. I. Eliason and L. K. Ferguson (*Surg Gynec and Obst.* 58:85 (Jan) 1934). From the results obtained in the treatment of *epiphyseal injuries* the authors draw some conclusions which may be useful in the future management of such cases: (1) Perfect reposition of the displaced epiphysis does not necessarily insure subsequent normal growth. (2) In most instances in which a single epiphysis forms the joint surface, partial reposition of the epiphysis was followed by normal subsequent growth (from 2 to 8 years). This statement is particularly true of the lower radial epiphysis. Especially in the younger age groups, nature seems able to compensate for considerable displacement. (3) Perfect reposition is most desirable in those areas in which several ossification centers are involved in the formation of the entire epiphysis, *e. g.*, lower humeral epiphysis. Displacement of these epiphyses and subsequent abnormal overgrowth may give marked impairment of motion in such a complicated joint. (4) Injuries in the region of the joints during the age of growth, even in the absence of x-ray evidence, should be considered possible epiphyseal separations without displacement. Treatment should be carried out with this possibility in mind. (5) The prognosis of epiphyseal injuries should be guarded because of the danger of premature ossification and because the extent of the injury cannot always be determined at the time of injury.

Fractures of the *humeral condyles* in children are the source of poor results much more frequently than realized. J. S. Speed and H. B. Macey (*J. Bone and Joint Surg.* 15:903 (Oct) 1933) and W. Avellan (*Acta chir. Scandinav.* (Supp. 27) 73:1, 1933) present excellent papers and are, in the main, in accord. Avellan describes 4 types of fracture of the lower end of the humerus, *i. e.*, the supracondylar fracture, fracture of the median epicondyle and condyle, fracture of the lateral condyle, and dicondylar fracture.

The frequency of the *supracondylar fracture* in children is explained by the late ossification of the epiphysis which is responsible for a difference of elasticity in the lower end of the humerus. Supracondylar fractures of the humerus are usually due to falls in which direct force plays a minor and indirect force a major part. They occur 5 times more frequently on the left side than on the right side. As a rule, the line of fracture, as seen anteriorly, runs almost transversely and often also slightly upward, and as seen laterally, runs slightly upward from before backward. The distal fragment is usually displaced posteriorly and medially. Of 31 cases, 28 showed a diminution of from 3 to 28°, 1 an increase of 11°, and in 2 there was no change in the valgus. Sixteen showed cubitus varus. The

chief cause of the frequent diminution of the valgus is the supination applied during reduction and fixation.

In 94.4 per cent. of cases the flexor-extensor mobility of the elbow joint is diminished by an average of 12.5 per cent., especially on extreme flexion and extension. In 6 of the cases reviewed, extreme extension was greater, the distal fragment healing with a more or less marked diminution of the normal axial angle anteriorly because during the reduction and fixation too little flexion was applied.

After such a fracture the lower end of the humerus and its articular portion are almost always greater than normal. In 15 of 30 cases there was an elongation of from 1 to 10 mm., and in 4 cases a shortening of from 1 to 5 mm., of the upper arm. In 11 cases there was no change. In 9 cases the circumference of the upper arm remained unchanged, in 2 cases it was increased from 5 to 7 mm., and in the remaining 20 cases it was decreased from 1 to 10 mm. A developmental acceleration was often noted in the ossification centers after the fracture. Especially abundant callus formation was found after unsatisfactory reduction and late reduction.

The *treatment* of supracondylar fracture consists of **reduction under anesthesia** with flexion of the elbow joint and pronation of the forearm. Special attention must be paid to restoration of the normal valgus and the normal anterior axial angle. The shoulder and wrist joints must be immobilized and the forearm pronated. If the x-rays show the reduction to be unsuccessful, **wire extension** to the olecranon or to the proximal portion of the ulna in vertical suspension is indicated. Surgical treatment is indicated only in nerve and blood-vessel complications and the so-called completely neglected cases. Early mechanotherapy is contraindicated, but **active motion**, not including the fixation area, should be begun as early as possible.

In fractures of the *median epicondyle and condyle* in which the dislocation is *slight*, good results are obtained by **conservative treatment**. If the dislocation is *marked* and the fragment has penetrated the joint, **surgery** with special attention to restoration of the lateral ligaments is indicated. It is of little importance whether the fragment is fixed or extirpated. If the fragment is large, **fixation** is advisable, but must be done accurately. In cases in which a part of the median trochlear region is also avulsed, a poor result is to be expected. **Immobilization** in flexion and pronation are advisable at first for the relief of pain and hemorrhage. The flexion-supination position should be avoided.

In fractures of the *lateral condyle* in which the dislocation is very *slight*, **conservative therapy** is indicated. If the dislocation is moderate and non-operative reduction has failed to restore the fragment to its place, **surgery** is necessary. If the fragment can be easily restored to its place at operation and well fixed in position, **osteosynthesis** is indicated, but if the reduction and fixation of the fragment prove to be difficult and not exact, **extirpation** is indicated. If the dislocation is marked from the start, operation should be done immediately. After extirpation, the lateral condyle shows striking power of at least partial regeneration. Extirpation is indicated also when the visibility of the fragment

appears questionable. In *osteosynthesis*, **temporary nailing** may be done and silk and wire, but not catgut, may be used for suturing.

In *dicondylar fractures* nonoperative treatment can be used rarely and then only when the dislocation is very slight. If **osteosynthesis** is necessary in addition to **open reduction**, nailing should be given first consideration.

**BONES AND JOINTS. — CONGENITAL DEFORMITIES.** — The *Klippel-Feil syndrome* is reviewed by J. T. Nicholson and De F. P. Willard (Ann Surg 99 561 (Apr.) 1934). It is characterized by (1) limitation of the movement of the head, (2) a low margin of head hair; and (3) absence of the neck.

In 1919, Feil expressed the belief that a high spina bifida is the original lesion, and that pressure and trauma later in fetal life are responsible for the fusion and malformation. He recognized 3 types: (1) complete absence of a cervical spine; (2) partial numerical reduction of the cervical vertebræ; and (3) associated partial reduction throughout the spine.

Willard and Nicholson report 2 cases, both of which belonged in the second group of Feil's classification. In the first case there was a numerical reduction of the vertebræ, due to fusion.

In none of the 60 cases reported in the literature was there a history of familial malformation. The syndrome has occurred with about equal frequency in both sexes.

The malformation is apparently determined before the third month of fetal life. The posterior spina bifida is caused by later fusion of the posterior chondrification centers for the vertebral bodies or by lack of fusion of the chondrification centers for the laminae. Because of faults in the chondrification centers of the laminae, fusion of adjacent spinous processes occurs. The apparent or actual reduction of the cervical vertebræ is brought about by faulty or complete fusion of the body chondrification centers in the formation of the continuous mass of pericartilage with the occiput. An extension of this abnormal fusion probably accounts for the changes which may appear in the upper thoracic region.

Additional *variations* occurring in the reported cases of Klippel-Feil syndrome included: (1) fusion of atlas to the occiput, (2) fusion of the first 3 vertebral bodies with fusion of the spines of the third, fourth, and fifth cervical vertebræ, (3) fusion of the first and second cervical vertebræ with an intact third vertebra and fusion of the fourth, fifth, and sixth cervical vertebræ, (4) fusion of the third, fourth, fifth and sixth cervical bodies and of the sixth and seventh cervical and the first and second thoracic spinous processes, (5) reduction of the cervical vertebræ to 4; (6) fusion of all cervical vertebræ in one mass with 4 cervical ribs and reduction of the thoracic vertebræ to 8; (7) a posterior spina bifida occulta, which in some cases extended from the occiput to the thorax; (8) fusion of the 6 upper thoracic vertebræ, (9) fusion of first and second right ribs and of 2 ribs arising from the fourth left thoracic vertebra; (10) fusion of the fifth lumbar vertebra and the sacrum, (11) dorsal spina bifida occulta and sacra rachischisis; and (12) oblique bodies of cervical thoracic vertebræ with a hemi-vertebra and unfused laminae.

The *physical characteristics* are apparent absence or shortness of neck, a low hair line on the back of the neck, a nuchal depression, flaring trapezii, a high position of the shoulders, prominence of the occiput, a dorsal kyphos, high scapulæ, proximity of the chin to the sternum, a low nipple line, limitation of head movement, and absence of pain.

*Associated variations* include torticollis, asymmetry of the face, scoliosis, Sprengle's deformity, absence of the external auditory meatus, abnormalities of the upper extremities, atrophy of the left forearm and hand, club-hand, mental debility, and bimanual synkinesia or mirror movements.

The condition may readily be mistaken for tuberculosis of the cervical spine. The *differential diagnosis* depends upon: (1) absence of rigidity; (2) motion without pain; and (3) positive x-ray findings.

As to *treatment*, Heidecker has reported improvement in mobility after **gymnastic exercise**. Ryerson noted improvement in the patient's appearance in one case after **division of the trapezius**. **Massage** and **stretching** should be given a thorough trial early in the growth period, and the **associated deformities** of torticollis, scoliosis, and club-hand should be **corrected**.

**ACUTE SUPPURATIVE ARTHRITIS.**—*Treatment*.—F. L. Liebolt and G. A. L. Inge (Surg Gynec. and Obst. 60:86 (Jan.) 1935) report 36 cases treated by **incision** and **drainage** at the Hibb's Clinic. After an extensive review of the literature the authors find no unanimity of opinion as to the treatment of purulent joints. Should joints be incised, aspirated, drained, lavaged or immobilized? Treatment in this group of cases was by wide and as early as possible **arthrotomy**, with **soft rubber drains** sutured in place. *Postoperative treatment* consisted of gentle **passive motion** immediately **after operation** followed by **active motion** as soon as the patient was able to bear it. Drains were removed by watching the temperature chart, usually on the seventh to the twenty-first day. **Traction** was used in most cases in the inferior extremity. Weight-bearing was permitted on an average on the forty-fifth day.

Factors influencing final results are:

1 *Virulence of infection*—There were, of course, wide variations in the virulence of the infecting bacteria as is shown by the fact that one patient with a *Staphylococcus aureus* infection of the knee recovered after simple aspiration, whereas others with the same organism were prostrated with a very severe infection and ended with poor joints in spite of early and efficient treatment. Low virulence of the bacteria may account for some of the excellent results obtained in this series, but it cannot account for all of them. It may not be unusual to see a joint infected with the pneumococcus get well with aspiration, but this must certainly be an unusual event with the staphylococcus.

2 *Early diagnosis and arthrotomy*—There was little temporizing with purulent joints in this series. Arthrotomy was performed in each case as soon as was feasible after the diagnosis was made. The only delay was in the patient's getting to the hospital. The best results, in general, were obtained in those joints which had early diagnosis and early arthrotomy.

3 *Use of drains*—Far from constituting a misdemeanor, it is believed that the results in this series of cases will show that the use of soft rubber drains



into the joint cavity is one of the most helpful adjuncts in the treatment of pyogenic joints. The drains must be soft; they must not be large enough to cause pressure necrosis; and they should be withdrawn as rapidly after operation as the subsiding of the infection will permit.

4. *Traction*—It is believed that the routine use of traction in these cases has exerted a favorable influence. Traction helps to relieve pain, to prevent or overcome flexion deformities, and possibly to protect the articular cartilages if, as Phemister claimed, necrosis of this tissue first occurs at points of pressure in a suppurating joint. The traction apparatus must be so applied that it will not interfere with free motion at the joint. The simplest method is by means of an anklet and a weight over a pulley at the end of the bed.

5. *Motion*—A great deal has been written in the literature about active *versus* passive motion, much to the discredit of the latter. It would be ideal treatment in pyogenic joints to start frequent, prolonged, and complete active motion immediately after operation, but such treatment can be attained only in rare instances. Only a single case need be seen to appreciate the suffering undergone by a patient with such a lesion, and when the average age of these patients is recalled, it becomes obvious that too much cannot be expected of active motion.

*Passive motion*, extremely gentle in its application, never forced in its degree, repeated several times a day by the surgeon, is much more feasible, and almost if not quite as effective as active motion in the early postoperative treatment. Each joint in this series was thus treated, and active motion substituted for passive as soon as possible. Emphasis must be placed on the gentleness of this passive motion. The importance of *active motion* cannot be overemphasized, but at the same time the usefulness of passive motion should not be overlooked.

6. The main purpose in the treatment of acute suppurative arthritis is, of course, the evacuation of the pus by the most efficient means possible. The use of **drains** and of early **passive and active motion** was invaluable in accomplishing this in the present series of cases, and the fact that these methods, when correctly used, are not destructive to infected joints is demonstrated by the end-results here reported.

Conclusions based on the 36 cases reported. Twenty-two of the cases were bacteriologically proved and uncomplicated by bone infection. The end-results in this group were: 12, or 54 per cent, were excellent anatomically, symptomatically, and functionally, 5, or 23 per cent, were good, 1 was fair, and 2, or 9 per cent, were poor. Four cases were similar to the above except that they were not bacteriologically proved. Results in this group were, 2 excellent and 2 poor. Ten cases were complicated by infection of the bone at the joint. The results in these were much worse than in the above groups, there being no excellent results, and 5 failures due to ankylosis or dislocation. It is thus seen that the presence of bone destruction greatly increases the seriousness of this disease.

In general, the best results were obtained in those joints which had early diagnosis and early evacuation of the pus. Active postoperative motion cannot be depended upon as the sole method of continuous evacuation of pus from an infected joint, because of the extreme pain and the usually tender age of the patient. In obtaining efficient continued drainage in this series of cases, the most

useful adjuncts to **arthrotomy** were found to be the insertion of **soft rubber drains** into the joint cavity and **gentle passive motion** immediately following the operation. The importance of **active motion** after arthrotomy cannot be overestimated, and this was substituted for passive motion as soon as the patient could stand it. There were no deaths, no amputations, no septicemias; ankylosis occurred only in 4 cases in which bone destruction at the hip had occurred before operation. The *prognosis* for function in acute suppurative arthritis is good if the diagnosis is made early and this is promptly followed by arthrotomy and drainage. It is poor if treatment is delayed until bone destruction has taken place.

**GONOCOCCIC ARTHRITIS.**—*Pathology.*—Studies of the synovial fluid in 40 cases of gonococcic arthritis are reported by W. K. Myers, C. S. Keefer and W. F. Holmes, Jr. (J Clin. Investigation 13:767 (Sept.) 1934).

*Findings.* (1) When the joints became involved as a result of a gonococcic infection, the synovial fluid was either infected or noninfected. In either case the fluid had the characteristics of an exudate, as judged by both the total protein and cell content. (2) The total synovial fluid cell count was increased in both types of fluid, but, as a rule, it was somewhat higher in the infected fluids. There were, however, wide variations. (3) The differential cell count was of greater importance than the total cell count in the two groups of cases. In practically all, the polymorphonuclear cells predominated. In the noninfected fluids, the clasmatocytes, monocytes and lymphocytes were present in much larger numbers than in the infected fluids. (4) The nonprotein nitrogen content of the synovial fluid was the same as that of the blood, regardless of the presence of organisms or of a high cell count. (5) The sugar content of the synovial fluid varied with the level of the blood sugar, the number of leukocytes and the presence of bacteria. Of these factors, the first two were of greater importance than the third. (6) The results of gonococcus complement fixation tests on the synovial fluid and blood were in agreement. (7) The bacteriologic, cytologic and serologic tests were of the greatest value in providing information of diagnostic value. (8) The chemical examination of the fluid revealed no information of diagnostic importance. (9) While the prognosis, as far as complete recovery was concerned, was poor, the presence of microorganisms and a high leukocyte count were more often followed by chronic disease of the joints than when there was a low leukocyte count and a sterile fluid.

**ARTHRITIS OF HIP JOINT.**—*Diagnosis.*—R. W. Butler investigated arthritis of the hip joint in 97 children (Brit M J 1:951 (June 3) 1933) and found that 56 were tuberculous. Thirty-four were suffering from a transitory arthritis only, without any abnormality being shown by the x-rays at any time. Seven had a transitory arthritis as a reaction to a localized bone infection near the joint, without true joint infection. A transitory arthritis without x-ray changes is common in childhood and is frequently diagnosed as tuberculous. Sometimes it may be traumatic in origin, but more often it is infective, the infection being often secondary to a focus elsewhere in the body. The prognosis of this transitory arthritis is excellent. The author gives a follow-up of 22 of the patients for an average period of 3 years.

A transitory arthritis is difficult to differentiate from a commencing tuberculous infection of the joint. Clinically, the two may be identical and remain so for days or even weeks. The x-ray examination is negative in a transitory arthritis, except in the type due to a well-defined neighboring bone focus, but a negative x-ray picture does not absolutely exclude tuberculosis. As a matter of fact, the x-ray picture is seldom absolutely negative in tuberculous arthritis when first brought for examination. Of the 56 children coming under treatment for early tuberculous arthritis of the hip, there was only 1 whose roentgenogram at that time was absolutely negative. All the others showed bone atrophy about the affected joint, most of them with loss of the joint space as well, and many with bone destruction already progressing. With a completely normal roentgenogram, the diagnosis should be *transitory arthritis* rather than tuberculous. The earliest stages of a virulent pyogenic epiphysitis or pyemic joint may show a negative x-ray picture, but the differentiation of these from a transitory arthritis cannot be long delayed on both clinical and x-ray grounds. The x-ray picture in *pseudocoxalgia* will seldom be so near to the normal that differentiation from a transitory arthritis will give rise to difficulty. All doubtful cases of arthritis in childhood must be watched carefully and treated like an arthritis that is likely to be progressive.

**SPINE, ARTHROSIS DEFORMANS OF.** — *Pathogenesis.* — Every deformity of the vertebral column is characterized by changes in the articulation of the vertebral processes, according to F. Lange (München med. Wchnschr. 80 1133 (July 21) 1933). These changes are far in excess of the physiologic motility, and sooner or later the abnormality of the articular space becomes fixed. A part of the articular space may become wider and another part may be narrower or entirely obliterated, or the widening or narrowing may involve the entire space uniformly. The result of the positional changes is that the joints show wear prematurely and an arthrosis deformans develops early. The author stresses that arthrosis deformans is to be strictly differentiated from, and not to be confused with, spondylosis deformans of the bodies of the vertebra, the latter being caused by a degeneration of the intervertebral discs. The law of functional overburdening has the same significance for the development of the arthrosis deformans in the articulations of the vertebral processes as it has for the development of arthrosis deformans in the joints of the extremities, *i. e.*, the arthrosis commences at the sites of the greatest mechanical burdening, and in advanced cases the most pronounced changes exist likewise at these sites.

The author discusses the development of arthrosis deformans in various disorders of the vertebral column, in scoliosis, in kyphosis and in vertebral fractures. In the latter disorder the development is particularly rapid. The studies on the pathology of the vertebral joints also indicated the cause of the backaches that sometimes occur in corpulent women with increased sacral concavity. It was observed that the articular spaces of the lumbar vertebræ had become wider and that the articular processes had become somewhat dislocated. This makes it understandable that these women complained of fatigue or of pain in the sacral region and that the wearing of a support gives them considerable relief.

**BACKACHE.**—*Pathogenesis and Treatment.*—The English are returning more to **manipulative therapy**, according to their writings. T. T. Stamm (Guy's Hosp. Rep 84: 372 (July) 1934) points out the possibilities of manipulation of the back as a method of treatment. Only 2 purposes can be achieved by its employment: (1) The replacement in apposition of displaced articular surfaces in dislocations and subluxations; and (2) the breaking down of obstructions to movement.

Pain in the back may be produced by the stretching of fibrous or scar tissue, by localized pressure, as when two bony points become impacted, and by congestion, which acts by causing intercellular tension, as in the pain of inflammation. The pain associated with the *stretching of fibrous or scar tissue* is characteristic. It is induced by activity and becomes steadily worse until rest is taken. The pain associated with a *subluxation* is also of the first variety. As the articular surfaces are no longer in correct apposition, certain of the ligaments of the joint must be under increased tension and this may persist even at rest. The pain, therefore, tends to be of a more continuous nature, and the congestive element is frequently present. The pain of *localized pressure* plays a much less important part in these cases and is usually associated with gross organic changes. In most cases the affected bony projections may be identified either by palpation or by the x-rays, and it is found that movements which tend to separate them will relieve pain and *vice versa*. There is little scope for manipulation in the majority of cases of this type.

*Lower back pain* which has its cause in the congestion of inflammation is similar in character to pain in other parts of the body attributable to the same cause. It takes the form of a continuous ache, made worse by activity and persisting even during rest. It is not relieved by alterations of position. It is characteristic of this type of pain that a feeling of stiffness in the part is experienced after a period of rest, and the first movements are the most painful. Manipulation in cases of this character requires careful consideration.

In *subluxation*, **manipulation** affords the only rational line of treatment and gives satisfactory results. The majority of patients are afforded instant and complete relief. In *acute* and *chronic sprain*, the adhesions and scar tissue can be broken down by **manipulation** and full mobility restored. There are then no structures to be put on the stretch, and the pain is relieved. At this stage **exercises** are beneficial, because by their means the restored mobility is retained and adhesions are prevented from reforming. In *chronic strains*, the result of inadequate muscular function, **muscular reëducation**, together with the **correction**, after careful analysis, of **faulty posture** associated with and related to occupation is indicated. **Manipulative treatment** is merely an important incident in the general scheme.

In cases of *focal infection*, the infection is dealt with first. Then, if the pain persists, **manipulation** may be performed. The results in the majority of doubtful cases show that the pain is relieved considerably by the manipulation, indicating that no active inflammation was present. Cases of *sacroiliac contusion* derive no benefit from manipulation. Prolonged immobilization in a **plaster cast** would appear to be a more rational line of treatment.

In all cases of possible damage to bone or cartilage in which manipulative treatment is contemplated, preliminary x-ray examination is of the utmost importance. Manipulative treatment must not be undertaken for osteoarthritic cases, as complete ossification of the spine may occur. In *acute cases of true primary sciatica* and in those cases in which the pain has been present for only a short time, *manipulation should be avoided*. In *long-standing cases*, however, in which it is probable that the pain has been perpetuated by the presence of adhesions, it is not of itself a contraindication to **manipulation**, which is often followed by considerable relief from pain.

**TENNIS ELBOW.**—*Etiology.*—According to K. Boshamer (Munchen. med. Wchnschr. 81:870 (June 8) 1934), this condition is due to an irritation of the periosteum of the lateral epicondyle of the humerus and is often limited to the lower edge of the epicondyle. If it exists for longer periods, periosteal deposits may become demonstrable by the x-rays. The median epicondyle is rarely involved. The cause is either a single direct trauma of the epicondyle or a continuous overexertion of the group of muscles attached to the epicondyle. The condition is frequent in persons who overexert these muscles, such as tennis players, cobblers, glass-blowers, cabinet-makers, riveters, tinsmiths and washer-women. Observations on 40 cases convinced the author that the direct single trauma is more often the eliciting factor than the chronic irritation.

*Symptoms.*—The epicondylitis is characterized by a sensitivity to pressure of the region of the epicondyle, by a piercing and burning pain in the same region when the arm is stretched at the elbow joint to more than 160°, and by radiation of the pains into the upper and lower arm and even into the fingers. Myalgia frequently coexists with the epicondylitis, and it is surprising that it frequently involves the antagonistic group of muscles, *i e.*, the flexors. A circumscribed edema is present rarely.

*Treatment.*—The main object of treatment should be to eliminate irritation of the periosteum, *i e.*, every exertion of the extensor muscles attached to the epicondyle. A **splint** is applied to the upper arm and forearm while the elbow is bent at a right angle. Care must be taken that the wrist joint and the fingers are completely extended, however, if the median epicondyle is involved, hand and fingers should be bandaged in the flexed position. To be able to influence the periosteal irritation with **diathermy** or with **ointments** that induce hyperemia, the author prefers the use of **plaster-of-Paris** splints that are fenestrated in the region of the epicondyle. Immobilization should be continued for 3 or 4 weeks.

**Hohmann's operation** may be resorted to, because it produces results in a comparatively short time. Under local anesthesia an incision 3 cm. in length is made over the epicondyle. The musculature on the anterior and lower rim of the epicondyle is notched and then the cutaneous wound is closed. The *after-treatment* consists of a **splint bandage** left on for only about 10 days. This operation should be resorted to (1) in case of long duration of the disorder, (2) when the disorder is caused by the occupation of the person, and (3) when the conservative treatment fails. In the majority of cases the conservative treatment will bring the desired results. Similar conditions mentioned by the author

are epicondylitis of the femur and tibia, periostalgia of the spinous processes of certain vertebræ, radial styloiditis and pressure periostalgias.

**KNEE JOINT DISORDERS.—*Diagnosis.***—Pneumoroentgenography of the knee joint is described by J. Oberholzer (Beitr. z. klin. Chir. 158:113 (Aug 16) 1933) After discussing the limitations of various existent methods, the author describes his method which is a combination of positive and negative contrast mediums. A small amount, 2 or 3 c c, of the positive contrast medium was injected into the knee joint and distributed by massage, after which the joint was filled with oxygen gas. The positive medium coats the joint capsule, the menisci, the crucial ligaments, and the cartilage. The introduction of the negative medium further intensifies the delineation of structures. Of the positive mediums experimented with, sodium iodide was found too irritating to the synovial membrane, while sodium bromide did not give sufficient contrast. Iodized oils were incapable of fine division and frequently clumped into masses which gave rise to erroneous interpretations. Iopax proved to be too painful. *Methiodal* seemed to possess all the qualifications required. It is nonirritating, is capable of fine division and gives satisfactory shadows. In Bircher's clinic, 700 arthro-pneumoroentgenograms have been carried out by the use of the combination of *methiodal* and filling of the joint with oxygen gas.

The author concludes that pneumoroentgenography of the knee joint is a safe procedure. It gives a clear presentation of the structures of the normal knee. It permits of recognition, in a high percentage of cases, of injury to the menisci, the crucial and lateral ligaments, the joint capsule and the Hoffa bodies. The diagnosis of Laewen's disease and of osteitis desiccans is placed on a more secure basis. Diseases of the capsule can be diagnosed with frequency. Follow-up observations with this method demonstrated a partial or complete regeneration of a resected meniscus in a majority of cases after a lapse of about 2 years. The method has its limitations and not all the types of trauma or joint disease are rendered recognizable by it.

**ARTICULAR CARTILAGE INJURY.**—Contusion of an articular cartilage is described by J. A. Key (Surg. Gynec. and Obst. 58:166 (Feb.) 1934) as a factor in chronic arthritis. Two cases are reported in which there was a history of trauma, and there was present pain, disability and swelling without locking. X-ray examination was negative. The knee in each case was explored and on the lateral condyle of the articular surface of the femur an area of necrotic cartilage was found, in one case about 2 cm. in circumference. This was removed with subsequent clinical improvement.

**OSGOOD-SCHLATTER DISEASE.—*Treatment.***—The treatment of Osgood-Schlatter disease with **drill channels** is reported by E. J. Bozsán and T. J. O'Kane (J. Bone and Joint Surg. 16:290 (Apr.) 1934). The rationale is based upon the theory that the fresh blood supply conducted to the diseased areas of bone facilitates and hastens the process of repair. A small incision or stab wound is made over the affected tibial tubercle and 1 or 2 channels are drilled through the diseased area indicated on the x-ray picture into the cancellous upper end of the tibia. Immobilization in casts appears to be unnecessary. The patients are allowed to walk as soon as they are able to do so without pain.

The authors treated 6 cases in this manner with prompt results. The clinical symptoms subsided within from 3 to 4 weeks and complete bony restoration has been demonstrated by x-ray examination as early as 7 weeks after operation. During this time pain and swelling have disappeared; the patients have regained confidence in the extremity and have been able to assume a squatting position.

The authors stress the fact that they recommend this operative procedure only for cases in which the handicap is severe and there has been long continued, serious annoyance with recurrent attacks of pain over a long period of time and for instances in which one or more years elapse before the symptoms subside entirely.

**POST-TRAUMATIC BONE ATROPHY OR SUDECK'S ATROPHY.**—This condition, which is discussed by F. B. Gurd (Ann Surg 99:449 (Mar) 1934), is a type of bone atrophy to be contrasted and distinctly separated from the demineralization uniformly accompanying fractures, long illnesses, or paralyses. It has been called "post-traumatic painful osteoporosis."

**Etiology.**—Bone atrophy is the result of (1) deficient nutrition, (2) disuse; (3) senility; (4) acute reflex (Sudeck's), (5) neuropathy. It is believed at present to be due to a paucity of blood supply in a sense of increased capillary and venous pressure which results in a local accumulation of carbon dioxide and stimulates osteoclastic absorption of bone.

**Theories.**—According to Sudeck (1920), it is a low grade inflammation; though Vialleton (1922) in histological specimen failed to find inflammatory reaction. Disuse atrophy presents a well-known picture, and this type must require some other factor. In experiments, circulatory interference plus disuse have not reproduced the picture. Bone atrophy does not follow local venous congestion or local anemia, so that the present theory is "reflex trophic neurotic," or, in other words, reflex arc stimulation as a result of local pain.

**Clinical Course.**—This is typical. A few days after a trivial injury, the foot or hand, which has been somewhat swollen and painful, becomes progressively more swollen and painful. Although possible to palpate pulse at ankle or wrist, the capillaries are engorged and an increased interstitial tension has occurred. The skin loses its markings and becomes "glossy." The joints become stiff and motion painful. Pain yields to absolute immobilization and in a few weeks x-rays show a very "patchy" atrophy of the bones in the immediate neighborhood and also in the bones distal to the site of injury, viz., lower one-third of tibia and fibula, lower part of radius and carpals, both scapula and upper parts of humerus are seen to be the site of osteoporosis. The course is divided into

(a) *Onset*—First appearance of patches on the x-ray picture.

(b) *Height of disease.*—Irregular areas of rarefaction disappear and the bones become uniformly permeable to the x-rays.

(c) *Reorganization*—Slow reappearance of calcium in the bones.

Oscillometric readings are reported to be 6 times stronger in affected areas than in the opposite normal extremity.

**Diagnosis.**—This depends upon loss of function and pain out of proportion to the original trauma and principally upon the x-rays. In the second stage, tuberculous osteoarthritis may be considered.

**Pathology.**—There seems to be a uniform loss of bony substance and not merely a depletion of the mineral salts of the bones, *viz.*, a diminution in the number and thickness of the bony lamellæ. Muscle, ligamentous and cartilaginous changes also accompany.

The principal site is the carpus and tarsus, with halisteresis of the epiphyseal ends of adjacent long bones. It is also reported in the shoulders, spine and skull. The age has varied from 21 to 58 years.

**Treatment.**—The process is reversible and patience is required.

1 *Prophylactic* **Surgical casts**, applied early in fractures

(a) *Lower limb* **Confine to bed; elevate limb 3 days; apply nonpadded cast**, and, when dry, allow **modified weight-bearing** by strapping felt on sole

(b) *Upper limb*. (1) **Cast**. (2) **Controlled diathermy** with patient moving wrist within limits of pain Do not manipulate.

Leriche advises **sympathectomy**.

**OSTEOMYELITIS.**—Acute osteomyelitis is considered by J. Fraser (Brit M. J 2: 539 (Sept. 22) 1934), who suggests that the localization of an abscess in the bone-marrow, although creating a "difficult and regrettable situation as far as the local infection and suppuration are concerned," may have a salutary effect, as it may be the body's method of producing a defensive area from which the factors of immunity may be developed. He argues that a general blood-borne infection may have less serious consequences if the infection becomes localized in a bone abscess. As there is a growing belief that the reticulo-endothelial tissue is one of the most important defensive mechanisms of the body, the fact that this tissue is concentrated in the metaphyseal areas of the long bones explains the frequency of the localization of bone infection in those areas.

**Treatment.**—In discussing the **operative treatment** of acute osteomyelitis, Fraser (*Ibid*) states that he is conservative. He advocates the **Starr technic**, though in a form even less extensive than that advised by Starr. He is disappointed with the gutter operation and is opposed to all the more radical procedures with wide débridement or subperiosteal resection. In the bone involved by acute osteomyelitis he makes numerous  $\frac{1}{8}$  inch drill holes up to the healthy bone area, using a freshly sterilized drill for each hole, to avoid extending the infection. The wound in the periosteum and soft tissue is left entirely open and lightly packed with sterile gauze soaked in a solution of liquid paraffin, acriflavine, and potassium citrate. The limb is then immobilized in plaster for 2 weeks. At the end of that time a dressing is done under anesthesia, the wound repacked, and plaster applied for from 4 to 6 weeks. On removal of the plaster the wound is reexamined, any sequestra formed are removed, and an attempt at partial closure is made.

Following the war, 3 standardized methods for the treatment of chronic osteomyelitis were developed, *viz.*, the **Carrel-Dakin method**, the **Orr technic**, and the **Baer's maggot treatment**. J. Buchman (Ann Surg 99: 251 (Feb)



1934) states that ideal treatment meets the following requirements: (1) thorough surgical removal of all diseased tissue; (2) efficient and continuous sterilization of the new wound, (3) efficient and continuous removal of wound discharges and dead tissue; and (4) stimulation of the formation of granulation tissue so that the cavity will be entirely filled before scar tissue contraction sets in

The *Carrel-Dakin* method meets only two of these requirements, *vis*, thorough surgical removal and washing out of dead tissue. The *Orr method*, in addition, produces self-sterilization of the wound by the formation of bacteriophage under the vaseline packs. Albee introduces stock cultures of **bacteriophage** during the operation

The **maggot treatment** meets all the requirements. The maggots remove microorganisms and small sloughs by ingestion; form a proteolytic enzyme which dissolves all dead matter, and by crawling about in the wound, irritate it sufficiently to stimulate the rapid growth of granulation tissue

There are numerous objections to the advantages of the maggot treatment, *vis*, expense of sterile maggots, technical difficulty of obtaining sterile maggots, the mental attitude of the patient, and, at times, local pain due to scavenging. M. A. Stewart (Surg Gynec and Obst 58:155 (Feb) 1934), following Baer's suggestion that some biochemical action, of which he knew nothing, was responsible for the favorable results, discovered that maggots excrete a high concentration of calcium ions. Reducing this principle to a technic, he advises the following treatment for chronic osteomyelitis: (1) Sound **surgical procedure** followed by **packing** for 24 hours. (2) Spray 3 times weekly with 0.25 per cent saturated aqueous solution of **picric acid in 8 per cent glycerin**. (3) Then spray with **calcium carbonate solution** ( $\text{CaCO}_3$ ), (gm 20—5 drams—to water, 215 cc—7 ounces)

This produced a local supply of calcium picrate with the theoretical advantages of calcium ions stimulating phagocytosis, alkalinity to counteract the acidity of the inflammatory reaction, and the analgesic action of the picrate ions. Following spraying, the wounds are packed open to prevent closure

Results claimed for the treatment are those of the Baer treatment, *vis*, it lessens the period of time for complete healing. In addition, it rids one of the disadvantages of the maggot treatment. L. B. Kline reports (Military Surgeon 75:251 (Oct) 1934) after using the Stewart treatment that granulation tissue forms promptly, purulent exudate is reduced, healing is rapid, pain and discomfort are minimized and the residual scar is less marked. He encourages **free exercise of the affected part**. The almost complete absence of pain permits of better cooperation. He has used these mixtures in the treatment of ordinary infected wounds with satisfactory results.

**MUSCLES.—PSEUDOHYPERTROPHIC PROGRESSIVE MUSCULAR DYSTROPHY.**—Since the work of A. T. Milhorat, F. Techner and K. Thomas (Proc Soc Exper Biol and Med. 29:609 (Feb) 1932) showing that patients with pseudohypertrophic muscular dystrophy have a creatinuria even on a creatin-free diet and suggesting glycine for treatment, many papers, most of which report favorable clinical improvement, have appeared

A critical review of **glycine therapy**, with biopsies taken before and after treatment in 9 cases, is reported by J. G. Reinhold, J. H. Clark, G. R. Kingsley, R. P. Custer and J. W. McConnell (J. A. M. A. 102:261 (Jan. 27) 1934). Biopsies, as a whole, provide considerable evidence for regeneration of muscle, and none that indicates further deterioration and, though based on a few numbers, results favor the view that improvement in the muscles actually had occurred. Clinically, the improvement has not progressed to the extent that might be expected from the indicated change in the composition of the muscle. The results are sufficiently indicative of improvement to suggest a continuation of glycine therapy. They conclude that little tangible evidence of improvement in muscular function has been obtained.

Muscle specimens removed at biopsy after treatment were distinctly better in quality, chemically and histologically, than similar specimens taken before treatment. Restoration of various characteristic muscle components accompanied regeneration of the muscle fibers.

**High protein diets, beef extract and gelatin** proved to be helpful supplements to glycine. **Ephedrine** has been of value in 1 case.

Despite the marked improvement in the structure and composition of the muscles in progressive muscular dystrophy after treatment with glycine (as indicated by examination of the biopsy specimens), a great disparity with the normal remained, probably sufficient in many cases to account for the failure of muscular function to be restored to a greater extent. The possibility of inducing further regeneration, perhaps sufficient to bring about unquestioned clinical improvement, remains to be tested.

**ANTERIOR POLIOMYELITIS.—*Prophylaxis.***—Successful method for **vaccination** against acute anterior poliomyelitis is reported by John A. Kolmer, G. F. Klugh, Jr., and A. M. Rule (J. A. M. A. 104:456 (Feb. 9) 1935). The vaccine is prepared from the spinal cords of monkeys inoculated intracerebrally with the virus. After devitalizing sufficiently with sodium ricinoleate, the cord of a large monkey will immunize 40 to 75 children, depending upon the age. The first dose has been 0.25 c.c. for children less than 3 years of age and 0.5 c.c. for older children up to 15 years. Varying amounts are being given in the second and third doses.

***Treatment.***—In determining the value of **convalescent serum** in pre-paralytic poliomyelitis, A. E. Fischer (Am. J. Dis. Child. 48:481 (Sept.) 1934) observed that the outcome for the treated patients was no better than that for the untreated ones, if as good; while in the controls the disease was probably somewhat milder, he feels that no advantage was shown by the other group of 579 patients with poliomyelitis seen early in the course of the disease, of whom 477 were treated by injection of convalescent serum. A sufficient number of control cases should be obtained, as the author's present study has demonstrated that there is no proof that a physician is depriving his patients of an equal chance for complete recovery by not administering convalescent serum. Lacking a substitute therapeutic procedure, it would seem fair in subsequent epidemics to retest the value of potent serum in the preparalytic or meningitic stage of poliomyelitis, using, if possible, exactly parallel or alternate cases for control.

**BICEPS BRACHII.**—E. L. Gilcreest (Surg. Gynec. Obst. 58: 322 (Feb. 24) 1934) reports the common syndrome of *rupture, dislocation and elongation of the long head* of the biceps brachii.

The *causes* are:

1. Physiopathological and pathological causes:
  - (a) Degenerative changes, such as senility, arthritis, myositis and arteriosclerosis
  - (b) Acute infectious diseases.
  - (c) Chronic infectious diseases
  - (d) Neoplasms.
2. Physiological predisposition.
- 3 Occupation.
- 4 Fatigue.
- 5 Trauma.

These causes combine to produce roughening of the groove and destruction by friction, resulting in fraying. After 30, the vascular supply of the tendon is less rich and the tendon loses tensile strength. Occupations calling for stress also cause wear and tear as the result of excessive fatigue. Rarely is rupture produced by violent muscular exercise.

The *sites of rupture* are:

- 1 High type—intracapsular.
- 2 Low type—at the level of the bicipital groove.

Ruptures are also:

- 1 Acute, in which medical aid is sought early
- 2 Latent, in which the fasciculi break slowly

*Subjective symptoms* are:

- a Variable in character, such as pain, audible as palpable snap
- b Constant is weakness.

*Objective symptoms* are found in altered shape of arm, local tumor, result of muscle shortening, hollow as hiatus result of tendon rupture, ecchymosis, result of hemorrhage, and a swelling of the contracted muscle. The last two are variable. Palpitation yields additional information. The tumor and hiatus are confirmed, the biceps is softened and has lost elasticity, and the tendon may have abnormal perceptibility. Function is impaired.

In *differential diagnosis* is mentioned *Yergason's sign*, which consists of flexing elbow to 90°, wrist pronated, when forceful supination elicits pain at the bicipital groove; and *Ludington's sign*, consisting of interlocking fingers on top of head to relax long head, followed by tensing biceps which obviates differences above mentions on the two sides (form, elasticity, tone, etc.) The syndrome should be differentiated from *muscle hernia of the biceps*, *subdeltoid bursitis* and *rupture of the supraspinatus*. Subdeltoid bursitis presents localized pain, worse on active or passive external rotation and abduction.

*Treatment* for the partial ruptures is to **immobilize** for 3 weeks in acute flexion. For the complete ruptures, **surgery** is the only treatment. Operative means that may be considered are:

- a Suture of the ruptured tendon to the short head of the biceps
- b. Suture of the ruptured tendon to the coracoid.
- c. To the pectoralis major.

d. To the intertubercular sulcus.

e. To the deltoid.

Probably the most satisfactory are a combination of (a) and (b).

In the lower ruptures the tendon should be reattached to the radius.

*Prognosis* in the partial ruptures is good with 2 to 3 weeks' rest. In the complete ruptures surgery is required.

Medicolegal appraisal is difficult and industrial liability depends upon:

1. History of recent trauma.
2. Immediate symptoms of injury.
3. Impairment of function.

For *treatment* of permanent paralysis of the deltoid, S. L. Haas (J. A. M. A. 104:99 (Jan. 12) 1935) discusses the advantages of **transplantation of the trapezius with a fascia lata prolongation into the humerus**. It is important to recognize and treat coexisting *dislocation* by the **Kiliani-Nicola operation**. Advantages over arthrodesis are:

1. Greater motion.
2. Less tendency to fracture.
3. Double arthrodesis in bilateral palsies is awkward.
4. Sometimes necessary to arthrodesis elbow on same side. Two contiguous joints are bad.
5. Better cosmetic result, especially in females, as the arthrodesis may cause the arm to project from the side.
6. For arthrodesis, the child must be 8 years or older. Transplant may be done earlier.

**OBSTETRIC PARALYSIS.—Treatment.**—For residual deformity in the upper arm type of obstetric paralysis, J. B. L'Episcopo (Am. J. Surg. 25:122 (July) 1934) advocates restoration of muscle balance to the shoulder in selected cases by making an external rotator of the teres major. Previous operations have aimed only at release of contractures.

*Technic*—The contracted anterior tissues are released by the Sever technic through the usual medial incision. After the wound is closed, a skin incision is made, from 3 to 4 inches long, parallel with the posterior border of the deltoid muscle and long head of the triceps. The incision is carried through the superficial and deep fascia, exposing the deltoid, long head of the triceps and teres major muscles. The long head of the triceps is retracted outward, exposing the tendon of the teres major muscle and the humerus. The tendon is freed at its insertion and detached. The dissection is carried out almost entirely with blunt instruments, to avoid injury to important structures. These structures are protected against injury if the operator keeps close to the teres major tendon throughout the dissection.

After the teres tendon has been cut, by inserting a blunt periosteal elevator in front of the tendon and cutting against it, the long head of the triceps is strongly retracted outward, exposing the posterior, lateral aspect of the humerus and the upper part of the origin of the lateral head of the triceps. An osteoperiosteal flap is then lifted from the shaft of the humerus as close to the short head of the triceps as possible. The tendon of the teres major is buried and sutured under this osteoperiosteal flap and the wound is closed in layers. A plaster-of-Paris spica cast is applied with the arm abducted and rotated outward with the forearm flexed and supinated. The new insertion is almost directly opposite the old one and the tendon wraps itself around the humerus from behind laterally instead of from behind.

medially, so that, when the muscle contracts, the humerus must rotate outward instead of inward

The cast is left on for 6 weeks, then cut open, so that it can be used as a splint; the splint is removed 3 times a week for massage and gentle passive and active exercises. The splint is discarded 3 months after the operation, but the exercises and muscle reeducation are continued for at least 6 months.

The author performed this operation on 6 patients with highly gratifying results.

**DUPUYTREN'S CONTRACTURE.—*Etiology.***—This is discussed by L. Gubern Salisachs (Rev. de cir. de Barcelona 6:81 (Sept) 1933). The lesion is a retraction of the palmar aponeurosis. The name "Dupuytren's contracture" is incorrect, as there is no pathological change in the muscles or tendons. The condition has been attributed to trauma, gout, rheumatism, chronic intoxication, embryological malformations, and other causes. From a study of 29 cases, Kanavel, Koch, and Mason came to the conclusion that it is due to a hereditary tendency.

The author reports 15 cases and concludes that the condition is the result of a funiculitis or neurodocitis of the extrameningeal tract of the nerve between the ganglion and the plexus, *i. e.*, through the vertebral foramen. In support of this conclusion, he cites the contracture of the vertebral muscles of the adjacent column causing segmental rigidity of the vertebral column in a number of his cases. He states that the spinal fluid findings are also significant. In radiculitis there is a lymphocytosis, whereas in funiculitis there is only a slight hyperalbuminosis. The cause of the funiculitis in the majority of cases reported was cervical arthritis.

The author believes that in all cases it is a trophoneurotic nervous lesion, but that it is not necessarily rheumatic. Similar lesions may be produced by syphilis, alcoholism, lead poisoning, and diabetes. Syringomyelia is a frequent cause of Dupuytren's retraction, and even very slight nerve lesions may produce the condition.

Dupuytren's lesion is uncommon. D. Macaggi (Polichinico (sez. Chir.) 40:743 (Dec) 1933) believes that trauma is not a factor in its development. He states that Mori found the condition in only 4 of 21,800 manual laborers, and he, personally, found it in only 5 of about 2000 industrial employees, such as miners, mechanics and metal workers. More frequent in the hands of such workers were changes that may be classified as pseudo-Dupuytren's contracture, as the hand subjected to repeated trauma tends to be somewhat flexed. The author attributes this flexion to a contracture of the tendons. Localized areas of thickening, nodules, and fibrous cords may also be produced by the chronic circumscribed irritation of an instrument.

**Diagnosis.**—According to D. Macaggi (*Ibid.*) Dupuytren's contracture is most common in males about 50 years of age. It is first manifested by a decrease in the extension of the ring and small fingers at the metacarpophalangeal joints. The changes in the middle finger are less evident, and the index finger and thumb are rarely involved. The condition runs a slow course. It usually begins in the more active hand. Often it is present for from 1 to 2 years before

contracture is evident, and from 6 to 12 years before the advanced stages of the disease are apparent.

The contracture is usually symmetrically bilateral, but is more pronounced in the active hand. When it is fully developed, the basal phalanges are forcibly flexed on the corresponding metacarpals and the middle phalanges on the basal phalanges, but the distal phalanges remain free. Associated with the flexion, there are longitudinal cords in the palmar aponeurosis, along the course of which irregular nodules and intersecting bands may be felt. Anatomically, sclerotic and atrophic changes are present in the palmar aponeurosis, skin, and subcutaneous tissues. The flexor tendons remain relatively uninvolved.

**Treatment.**—**Tendon grafting** for complicated contractures of the hand is reported by S. L. Koch (*Ann. Surg.* 98:546 (Oct.) 1933). Infections in the hand follow the tendon and muscle sheaths and the worst damage is found where the exudate has been under the greatest tension, as in the digital tendon sheaths and under the anterior annular ligaments. In attempts at surgical repair, it may be necessary to shorten a tendon, as, for example, when flexors become fixed in a relaxed position during acute infection. On the other hand, if the tendons have been contracted during the infection, they must be lengthened to restore function. Stiff joints must be mobilized before tendon surgery.

Tendon grafting is necessary for the bridging of gaps caused by extrature of the proximal fragment of a severed tendon; for cases in which infection has caused so many adhesions around a sutured tendon that it is impossible to free them and obtain a workable tendon; and for cases in which there has been a complete destruction of a tendon. In the finger, the bed is prepared for the tendon graft by removing all scar tissue and fragments of the old tendon. The author prefers free exposure by lateral incision to the tunneling advised by some surgeons. End-to-end suture of the graft to the tendon is the method of choice. It is better to attach the distal end of the graft directly to the bone after removing the distal fragment of the torn tendon. On the distal phalanx, instead of trying to drill the small bone for attachment, the tendon graft may be looped around the back of the bone and sutured to itself on the palmar side. For a gliding mechanism, the tendon graft, when removed from the foot, is taken with its surrounding areolar tissue intact, to preclude the necessity of wrapping with fat from another source. An annular ligament must be reconstructed at the second phalanx and at the middle of the proximal phalanx. This may be done by wrapping a free tendon graft around the phalanx, including the new grafted tendon, and holding it down to the bone. Strips of the sublimis tendon may be used instead of a free graft.

In order to make as easy as possible the procedure of attaching the tendon graft to the distal phalanx and of constructing new annular ligaments to hold it in its bed when tension is put upon it, the author has come to perform the various steps of the operation in a definite order.

After the remains of the scarred tendon have been completely excised, the graft is laid in place and attached to the distal phalanx. A silk suture is attached to the free end of the graft and passed through the tunnel left by the excision of the scar tissue over the proximal portion of the proximal phalanx and out through the palmar incision. With the graft laid

smoothly in the finger and held there by slight tension on its free end, the new annular ligaments are constructed. When they are completed it is possible, by putting tension on the proximal end of the graft, to see exactly how well they function and if they have been sutured under the proper degree of tension. The next step is closure of the incisions in the finger. The proximal end of the graft is then sutured to the distal end of the tendon in the palm. The final step is closure of the incision in the palm.

After this procedure the finger is put up in moderate flexion and the wrist in more pronounced flexion. Complete restoration to normal function cannot be expected in such cases, but the effort is worth while if a perfectly stiff finger can be given enough motion to render amputation unnecessary.

The chief causes of failure are infection, the pulling out of insertions into bone, fibrosis and adhesions of the graft to surrounding tissue, and adhesions or ankylosis in the joints. The attitude of the patient is an important factor. It is obvious that a patient who is determined to obtain maximum function will have a much better result than one who desires motion to be minimal in order that he may obtain maximal financial compensation. It has sometimes been observed that results which were not very encouraging when the patient left the surgeon's care become much better with subsequent use of the finger.

**WRY NECK.—Treatment.—Operative treatment** of wry neck is reported by W. Arnold (*Arch f klin Chir* 178 257 (Dec 15) 1933). Sixteen patients were operated on between 1919 and 1924 by the **Volkman method** of open tenotomy of the lower ends of the sternocleidomastoid muscle. From 1924 to 1931, 40 were operated on by the **method of Mikulicz**, which consists of partial or complete extirpation of the sternocleidomastoid muscle. A number of the patients came at a late stage, after the tenth year of life, when irreparable secondary changes have taken place. In 43 cases in which the obstetric history could be obtained 25 had been breech, 17 occipital, and 1 posterior parietal presentations. Much stress is laid on the *postoperative treatment*. This consists of **massage of the scar, passive and active exercises of the neck**, and certain **special gymnastic procedures**. The functional *result* after the Mikulicz operation was far superior to that of tenotomy. There were 2 failures after 14 tenotomies and only 1 failure after 35 Mikulicz operations.

Since 1931, the author has had experience in 9 cases with the **method** advocated by **Lange** and by **Tillaux**. It consists of sectioning the upper end of the sternocleidomastoid muscle just below the mastoid process. The advantages claimed for it are (1) a scar that can be concealed by the hair, (2) preservation of the contour of the neck and avoidance of a depression just above the clavicle, (3) better functional result, and, (4) a smaller operation without accidental injuries (jugular vein; the accessory nerve). Of the 9 cases, 7 presented excellent results, 1 was improved, and 1 was a failure. The author feels that in the future he will prefer the Lange-Tillaux procedure for the cases belonging to Group 1 of Lorenz as well as for the milder cases of Group 2 of Lorenz up to the age of 15 years. Past this age, the procedure must depend on the severity of the case. For the more *severe cases*, **partial or complete extirpation of the sternocleidomastoid muscle** holds out the prospect of a better functional result. Better results may be expected with individualization of the operative method rather than by adhering to any one scheme.

# Thoracic Surgery

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**TUBERCULOUS EMPYEMA.—*Etiological Considerations.***—With the increasing use of pneumothorax therapy there is a corresponding increase in the possibility of development of tuberculous empyema. V. V. Pisani and F. J. Smejkal (Tubercle 15:216 (Feb.) 1934) say that in 50 per cent. of therapeutic pneumothorax cases followed through from start to finish show fluid at some time. Happily, by far the majority of such cases go on to absorption without the development of frankly purulent tuberculous exudates or of the more serious mixed infection exudations. With, however, the hazard of the tearing of an adhesion ever present or of accidental lung puncture by the aspirating needle, the possibility of added pyogenic infection from within is a not negligible possibility, and calls for the greatest care in pressure estimations and gradations of refill amounts in all cases throughout the whole course of treatment. Nor is the possibility of introduction of pyogenic organisms from without to be disregarded, as M. Joannides (Am. Rev. Tuberc. 29:313 (Mar.) 1934) has indicated; but with all precautions having been observed, cases of tuberculous empyema or of empyema in tuberculosis will occasionally have their origin in pneumothorax therapy, and others which have developed in the course of recognized or unrecognized tuberculosis will present themselves for treatment

***Classification.***—To make clear the individual group problems, J. C. Jones and J. Alexander (Am Rev. Tuberc. 29:230 (Feb ) 1934) have classified their cases, according to the method of Hedblom, into 4 groups:

*Group I.* Includes cases of *pure* tuberculous empyema *without* pulmonary tuberculosis.

*Group II.* Includes *mixed* tuberculous and pyogenic infection *without* demonstrable pulmonary tuberculosis.

*Group III.* *Pure* tuberculous empyema *with* clinically active pulmonary tuberculosis

*Group IV* *Mixed* tuberculous and pyogenic empyema, with active pulmonary tuberculosis.

***Complications.***—In the group of 70 cases summarized by Jones and Alexander (*Ibid*) it is shown that the empyema at the time of admission was complicated by *mixed infection* or by *active tuberculosis*, or both, in 69 cases, and that 17 had *bronchopleural fistula*. The proof of tuberculosis was definite in 65 by finding tubercle bacilli in the aspirated fluid, or by direct smear or by guinea-pig inoculation, or by finding characteristic tubercles microscopically in a portion of the parietal pleural scar that was routinely removed for examination in those cases which were openly drained. The 5 cases in which tuberculous empyema was not absolutely established belong to Group III, which consists of pure tuberculous empyema, with associated active pulmonary tuberculosis. The records do not show that tubercle bacilli were demonstrated in the aspirated pus from these 5 cases, but in all of them the empyema complicated pneumothorax that was induced for cavernous pulmonary tuberculosis with tubercle bacilli in the sputum, the writers consider that these 5 empyemata were tuberculous

***Prognosis.***—Jones and Alexander (*Ibid*) state that it is not unusual to hear sanatorium physicians say that in their experience the mortality in the mixed

tuberculous and pyogenic type of empyema has been between 90 and 100 per cent. and that they have never had a patient who became genuinely cured. It is our thesis in this article that the successful management of tuberculous empyema demands the use of one or more of several procedures and that the treatment of each patient must be highly individualized.

Recently the writers have traced every one of 70 consecutive patients and found the following results: Cured, 54.3 per cent.; improved, 85 per cent.; not improved or worse, 43 per cent.; dead, 32.9 per cent. By cured is meant that the empyema cavity is completely obliterated and that no sinus remains and that, if pulmonary tuberculosis was present, sputum is now absent or it contains no tubercle bacilli. All of the patients listed as improved are still under treatment.

**Treatment.**—A *Group I* case is a relatively unusual finding, *i. e.*, a pure tuberculous empyema without mixed infection or evidence of active pulmonary tuberculosis. The purpose of the treatment, according to Jones and Alexander (*Ibid*) is to bring about expansion of the lung with consequent obliteration of the empyema cavity. This should be accomplished by **repeated aspirations**, perhaps with **temporary partial air replacement** and virtually never by closed or open drainage because of the almost certain addition of pyogenic infection to the empyema. **Extrapleural thoracoplasty** should be performed only in the event that a reasonably prolonged trial of aspiration should fail to result in complete expansion, but not in every case if the pus is stationary and the patient asymptomatic.

In *Group II*, *i. e.*, patients with mixed tuberculous and pyogenic empyema, but without evidence of active pulmonary tuberculosis, the object is to evacuate the pus because of its content of pyogenic organisms, and to expand the lung because of the empyema cavity. This may occasionally be accomplished by **repeated aspiration** with or without **irrigations** or **instillations** of dyes, **gomenol** or other chemical substances, a closed or preferably open **drainage** usually becomes necessary. A **phrenicectomy** is useful to assist in obliteration of the empyema cavity, and this should be performed early, so as to cause a rise of the diaphragm before it becomes fixed by a rigid pleural scar. If aspiration, drainage and phrenicectomy fail to close the cavity completely, and if the open cavity finally shows no disposition toward progressive closure, an **extrapleural thoracoplasty** and painting of the costal periosteum with a 10 per cent **formalin** is the treatment of choice. Should a residual cavity remain several months after the extrapleural thoracoplasty, it may be obliterated by a one or more-staged **Schede thoracoplasty**.

In commenting on the origin of this group of cases the authors make the following statement which must emphasize to all the absolute necessity of the correct classification of the case before surgery is initiated: It is estimated that certainly not more than 15 per cent., and probably fewer, of these patients had a pyogenic infection complicating their empyema before the initial drainage was performed, and that the great majority of the pyogenic infections that were present when the patients of this group were first seen, were directly brought about by the mistake of draining a purely tuberculous empyema. The diagnosis

of tuberculosis was first made at the University Hospital in 92.9 per cent. of these 14 patients

In *Group III* are patients with pure tuberculous empyema, without associated pyogenic infection but with active pulmonary tuberculosis. The object of treatment is twofold: To stop the formation of pus in the pleural cavity and usually to maintain collapse of the tuberculous lung.

The simplest measure that may succeed is **repeated aspiration with air replacement**, thereby maintaining the collapse of the lung by pneumothorax. A **phrenicectomy** helps to maintain collapse, especially if there is a tendency toward obliterative pleuritis. In such cases **extrapleural thoracoplasty** is clearly the treatment of choice, according to Jones and Alexander (*Ibid.*), if there is no specific contraindication to it. If in such cases a needed thoracoplasty is contraindicated, **phrenicectomy** and **continued aspirations** may palliate the symptoms. If a patient is highly toxic and does not respond properly to simple aspirations, repeated cultures should be made of the aspirated pus and these should be promptly incubated.

In *Group IV* are those patients with mixed tuberculous and pyogenic empyema, with associated active pulmonary tuberculosis. The objects of treatment are to evacuate the pus and sterilize the empyema cavity and usually to maintain collapse of the diseased lung. Closed or open **drainage** should be instituted early when a brief trial of aspiration fails to do more than slightly or temporarily improve the patient. As in Group III, **phrenicectomy** should usually be used early to relax the diseased lung and lessen the size of the empyema cavity. For those cases in which permanent collapse is desirable, and particularly for those in which prolonged drainage has resulted in improvement in the general condition, but in only partial obliteration of the empyema cavity, a **thoracoplasty** is highly desirable. An **extrapleural thoracoplasty with formalinization of the periosteum**, will either obliterate the cavity or reduce its size. If, after several months, a residual cavity should remain, it may be closed by a less extensive **Schede thoracoplasty** than would have been necessary had an extrapleural thoracoplasty not been first used.

In a final *summary* of the question of tuberculous empyema, Jones and Alexander (*Ibid.*) state they believe that attainment of good results in tuberculous empyema depends chiefly upon recognition of the importance of distinguishing between the 4 absolutely distinct types of the disease and upon a high degree of individualization in the application of the therapeutic measures that may be properly applied in each type. Reliance upon nothing but prolonged aspirations, with or without antiseptic irrigations or instillations, and without regard to the type of empyema being treated, inevitably results in a shockingly high mortality. An important cause of failure in those cases in which tube-drainage has been used is that frequently the tube is not placed at the most dependent part (with reference to a recumbent patient whose shoulders are slightly raised by pillows) of the empyema cavity, and that the tube is either too long, too short or too narrow, and particularly that the tube is removed before the cavity has become completely obliterated. Another cause of failure is that many of the thoracoplasties

that are being performed for empyema are not planned to give maximal assurance of complete obliteration of the cavity and they are performed in so few stages as to make the operative mortality frightfully high.

### **PULMONARY TUBERCULOSIS.—SURGICAL TREATMENT.**

—Though a number of years have passed since the pioneer work in the surgical therapy of pulmonary tuberculosis was done, there is still considerable evidence of hesitation in the acceptance of these helpful *adjunct* measures of therapy. Again, it is to be emphasized that with the acceptance and application of surgical therapy, there is to be no relaxation in the administration of all other measures of treatment, whose use has been productive of the marked changes in end-results of the present day as compared with those of five decades earlier.

In securing maximal benefit from surgical procedure and collecting convincing evidence as to the value of the procedures suggested, 3 requisites are immediately to be noted:

(a) A proper selection of cases

(b) Correct application and completion of the details of the operative procedure.

(c) Collection of statistics of such mass and from competent sources, that the occasional very encouraging or disappointing results from small series of cases will be truly balanced by a great mass of figures.

**SELECTION OF CASES**—Many factors enter into the proper selection of cases. This phase of the problem is well indicated by F. M. Pottenger (Am. J. M. Sc. 188. 169 (Aug.) 1934). At the outset of his discussion he states that he wishes to make plain that there is no antagonism between nonoperative and operative measures in the treatment of tuberculosis. There is a vast difference in opinion as to when one or the other should be employed, but such antagonisms as exist are between partisan advocates of one or the other method. He discusses the curability of tuberculosis and attempts to point out the manner in which healing is accomplished. He also points out the factors which favor and those which prevent such accomplishment, and shows how treatment must be suited to each case and further shows how the correct treatment is conservative, whether it be operative or nonoperative.

If patients could all be treated in an ideal environment by physicians who not only understood tuberculosis, but who possess a mental attitude adapted to the treatment of chronic illness, and if the patients were so desirous of getting well that they would adhere rigidly to the necessary regimen, then the cure of early tuberculosis, like that of other infectious diseases, would be largely a matter of natural and specific defense, and only complicating conditions would require a deviation from the well-established hygienic, dietetic, open-air, rest regimen. Such, however, is not the case. These variants influence the success to be attained as much as the character of the treatment which is instituted to cope with the disease *per se*. Therefore the treatment of tuberculosis cannot be discussed from a purely scientific standpoint, but must include its psychologic, social, domestic and economic aspects.

A favorable result obtained by operative measures, therefore, does not necessarily mean that it could not have been attained by nonoperative measures, nor does one attained by nonoperative measures mean that it could not also have been attained by operative measures. The point at issue is, which method best conserves the interest of the patient, and this can be determined only after taking into consideration, and carefully weighing, the dangers that may come to the patient by not using some operative measure, and comparing them with any injury that may follow the employment of operative procedure.

In the natural healing of tuberculosis, reliance is placed by Pottenger (*Ibid.*) on the patient's own body reactions to bring about healing, the same as in all other infectious diseases for which there are no specific remedies. This protective mechanism differs with different individuals, both as to its efficiency and as to the time required for its development; but it is slow in all cases. This fact furnishes one of the chief causes of failure.

If a carefully devised program, suited to the patient's particular requirements, is carried out sufficiently long, according to Pottenger, it will assure success in nearly all of those cases in which healing depends upon the resistance of the patient. Nonoperative measures are insufficient, however, in patients in whom metastases continue to recur, in whom destructive lesions are uncontrolled, or in whom mechanical factors interfere so that rapid healing cannot take place.

The mechanical conditions which particularly interfere with compensation are pleural adhesions, fixation of the mediastinum, adhesions and fixation of the diaphragm, widespread fibrosis, the emphysema which has developed prior to the time of the destructive lesion and rigid thorax.

While the curability of tuberculosis depends upon the extent, age, and activity of the lesion, it again depends upon whether it is predominantly exudative. That there is a difference in exudative and proliferative tuberculosis has long been known, and recently the clinician has begun to understand certain of the fundamental causes of this difference. The fact of this difference must be considered in applying therapeutic measures.

From the purely scientific standpoint, in which the curability of tuberculosis alone is considered, the writer has found that the following types will heal fairly regularly without operative assistance:

- 1 Early limited lesions of either the proliferative or exudative type

2. Proliferative lesions more extensive than those mentioned under Group 1, involving one or both lungs, providing they have not taken on extensive metastases and destructive processes with multiple cavitation.

- (a) Small cavities may usually be expected to heal, but the healing of large ones, especially if multiple, is more doubtful without operative aid

- (b) Whether or not such lesions will heal depends much upon the extent of injury which has been done to the lung tissue, and the ease with which the necessary compensatory changes between lung volume and intrathoracic space may be made

- 3 *Exudative* lesions more extensive than those mentioned in Group 1, with or without cavity, provided the noninfected lung tissue can take on the required emphysematous changes, and the mediastinum is free to shift, in case it is required by the compensation which must be made, and provided further that other limiting structures are able to accommodate themselves to the reduced lung volume.

Early cavitation in exudative tuberculosis is not a contraindication to healing, unless it is held open by pleural adhesions and a fixed mediastinum, or so located that it cannot close

4 Exudative lesions which are accompanied by extensive atelectasis will usually heal even though they may be accompanied by high temperature which requires several months to reach normal.

From the purely scientific standpoint, this leaves practically no early cases that require operative assistance, but, as the disease advances, there are several types of lesions which cannot be depended upon to heal without operative aid, some of which are the following

5. Comparatively small lesions with a cavity which is held open by pleural adhesions, and is prevented from closing because the unaffected lung tissue is not able to make the necessary compensatory changes, such as apical or subapical cavities covered by a pleural cap, and especially when the upper mediastinum is fixed

6. Any active lesion which continues to form metastases unduly long, in spite of carefully followed nonoperative treatment.

7 Lesions in which a destructive process is seriously threatening cavity formation; in fact, should cavitation threaten during the course of chronic tuberculosis, it should probably always be prevented by collapse, if possible

8 Any lesion which is prevented from healing by mechanical hindrances

This will include

(a) Small cavities situated so that the walls cannot collapse as in the apex covered by a pleural cap, small cavities in dense scar tissue situated in any part of the lung; and those near the hilum or diaphragm

(b) Extensive infiltration, with or without cavity, in which the tissues are put on marked tension, and in which compensation necessary to healing cannot be made

(c) Large cavities with thick fibrous walls.

(d) Cavities in a much contracted lung, with displaced mediastinum in which further compensation cannot be made

Pottenger has found that this grouping roughly separates the cases which may be expected to heal by nonoperative measures from those which require operative assistance. He states, however, that it does not represent the manner in which tuberculous patients are generally treated, because operative measures are so frequently found necessary to meet the exigencies under which treatment is carried out. Not only are groups 5, 6, 7 and 8 recognized as requiring operative aid, but some of group 1, many of groups 2 and 3, and practically all of group 4 are usually treated by pneumothorax or phrenicectomy or both

WHEN TO OPERATE—Besides such an anatomicopathologic grouping of the amenable and nonamenable cases, surgically speaking, there enters into the problem the difficulty at times in choosing the fortuitous moment for the case in hand. With this aspect of the matter in mind, H. Jessen (*J. Thoracic Surg* 4:1 (Oct.) 1934) states that first, tuberculosis is always a disease of the whole organism. It is a general infection with all its properties. We find the infectious focus in a toxic and metastatic sense on every occasion in the lymphatic system where it remains even if it becomes latent. Therefore each cavity must be considered a metastatic illness. Furthermore, human tuberculosis must be considered as an extremely individual problem on a constitutional and biologic basis. It is known perfectly well that tuberculosis can be a continual change between periods of inactivity and activity. Therefore, all surgical treatment has to adapt itself to the present condition and character of the disease, and it is understood that the right time for the surgical intervention depends first of all upon the general state of the body. Surgical intervention can be the immediate *conditio sine qua*

*non* for the patient; it can become advisable and only practical after a long period of preparation and treatment; finally, it may never become feasible. Sometimes it is very difficult to fix the right time, and only great experience can help to determine the exact moment for intervention.

A third point is referred to by Jessen. While "great surgery" is generally performed on healthy people, all thoracic antituberculosis surgery has to tackle an organism damaged by a chronically poisoning disease, with the serious consequences of toxic weakness of the heart and great vessel system. At the same time, surgery does not attack or eliminate the diseased organ, but it tries to imitate nature by establishing mechanical conditions necessary for fibrotic transformation of the tuberculous tissue.

Thoracic surgery must therefore unavoidably weigh and balance the extent of the whole problem, *i. e.*, the extent of the surgical intervention against the biologic endurance of the individual patient.

**OPERATIVE PREPARATION AND TECHNIC**—In considering the correct application and completion of the details of the operative procedure one is immediately aware of the very personal equation of thoroughness and breadth of vision which enters in with utmost importance when the major procedures, thoracoplasty in particular, are under consideration.

The immediate morbidity and mortality will be influenced by the preoperative preparation; transfusion, postural emptying of the cavities, as well as by the immediate operating room details, of type of anesthesia and expertness of administration, and operative technic as particularly concerns hemostasis. Postoperative treatment, in so far as transfusion and adequate provision to meet possible anoxemia, must have been provided for. The ultimate success, in actual final recovery from the disease, will require appreciation of the safe extent of the individual steps of the multistage operation, and of the efficiency of the total result on completion. The procedures carry the burden of responsibility over periods of weeks, rather than over the shorter periods of several days, as in the large percentage of operations of major abdominal surgery. An adequately managed convalescence for a sufficient length of time for the completion of the healing process is an important condition for the permanent arrest of the disease, in the opinion of C. A. Hedblom and W. Van Hazel (*J. Thoracic Surg.* 4: 55 (Oct.) 1934).

**MORTALITY**—The findings of Hedblom and Van Hazel (*Ibid.*) in their critical study of a group of almost 4000 cases of thoracoplasty published since the studies of Alexander, in 1926, show that the combined mortality rate, during the first 8 weeks postoperative among 3811 cases was 10.5 per cent, while the individual variations in the series were from 3 to 21 per cent.

Among 3762 patients followed for from 1 to 12 years after operation, 35.3 per cent were free from symptoms and bacilli and were able to work, 22.1 per cent were improved and able to do some work, 5.5 per cent were not improved or were made worse by the operation, 3.5 per cent were not traced; 33.6 per cent were dead at the time of the report. A large proportion of the patients were rehabilitated to the extent that they were able to return to their former stations in life, and to resume their former occupations or activities.



Many women married, and there is record of 22 who have borne children since their operation, usually against advice.

**Pneumothorax.**—With the continued use of pneumothorax there is a better understanding of its value and of its limitations. Particular attention is being given to the consideration of bilateral pneumothorax therapy, and to overcoming the obstacles to collapse, produced by adhesions, by the procedure of intrapleural pneumolysis. Methods of reducing the percentage of effusions during the continuance of gas therapy are also being given consideration.

In discussing the simultaneous *bilateral* artificial pneumothorax in the treatment of pulmonary tuberculosis, P. M. Mattill and T. J. Kinsella (J Thoracic Surg 4.13 (Oct.) 1934) report on a series of 120 patients in whom the procedure was attempted, and in 90 of whom bilateral collapse was demonstrable. The remaining 30 have been used as a control group. Of importance is the pathologic grouping, 2 presenting minimal, 39 moderately advanced, and 78 far advanced lesions on admission, but all were moderately advanced or far advanced at the time of the establishment of the bilateral collapse. The side presenting the most active or most destructive lesion, was the side first attempted in most instances.

INDICATIONS—1 *Extension to or reactivation of disease in the contralateral lung or failure of an original lesion to improve during unilateral pneumothorax.*—Mattill and Kinsella consider that in this condition constitutional rest and other means should certainly be given a fair trial. The establishment of a secondary pneumothorax ordinarily is more satisfactory and offers the patient a better chance of recovery than giving up the original pneumothorax and subsequently collapsing the second side.

The superiority of simultaneous bilateral over alternating pneumothorax with this type of lesion is emphasized again in this same series, in which 69 per cent of the patients who developed extension into the contralateral lung did so within 1 year, and 84 per cent within 2 years, periods of time considered by the writers to be too short to consistently afford ample assurance of complete healing in the original side if it was originally badly diseased.

2 *Primary bilateral pneumothorax for extensive bilateral disease*—Care must be exercised in treating patients in this manner not to establish collapse so rapidly that it causes distress and dyspnea. Individuals in whom the disease is so extensive that it has already markedly reduced the vital capacity should not be chosen for this type of treatment. The results obtained by the use of primary bilateral artificial pneumothorax in treating patients with acute exudative bilateral tuberculosis with extensive disease certainly do not warrant the selection of a large number of cases of this type in any series for bilateral collapse.

3 *Pulmonary hemorrhage*—The occurrence of pulmonary hemorrhage during unilateral pneumothorax at times raises a serious question as to its origin. Failure to control hemorrhage by increasing the original collapse, in case the cavity bearing area is not held out by limiting adhesions, should direct the attention to the contralateral side and suggest the use of a second pneumothorax as the solution of the problem if the hemorrhage persists. Collapse of the second lung may control hemorrhage coming from the second side and may possibly be of

value if the bleeding is known to be coming from the original lung. Rarely, contralateral collapse to such a degree that some mediastinal displacement is produced may add compression to the original lung in an adherent region not sufficiently collapsed by increasing the original pneumothorax.

[There were only 13 cases in the group of 120 in which hemorrhage was the indication. Unfortunately, no figures of any kind are presented concerning the immediate success of the measure considered indicated. Especially interesting would be a report on the contralateral injections. EDITOR.]

TECHNIC—Slow establishment and gradual increase has been followed, using relatively frequent (2 to 3 days) injections and small amounts (150 to 300 c.c.). It has been considered safer to give the refills on the two sides on different days in order to gradually produce the accompanying changes in vital capacity and circulation physics, as well as to avoid the possibility of an accidental pneumothorax developing on the two sides at the same time. The need of careful repeated fluoroscopic check is suggested by Mattill and Kinsella, particularly in those requiring extensive collapse in the presence of a flexible mediastinum.

AFTER-CARE—In the opinion of Mattill and Kinsella (*Ibid*) all patients carrying bilateral artificial pneumothorax are sufficiently ill to justify constitutional treatment (**bed rest**) at the same time. Bed rest is of value also by reducing the patient's respiratory needs and thus permitting the maintenance of a more extensive collapse at a time when it is necessary. Vital capacities below 1000 c.c., as low as 25 to 30 per cent of the theoretical normal, have been maintained for a considerable period of time with the patients at rest without discomfort.

RESULTS OF OPERATION—As an indication of the general stability of some of the patients under this treatment, Mattill and Kinsella (*Ibid.*) record that 2 individuals in this series have not only carried a bilateral pneumothorax of considerable proportions, but at the same time have had the diaphragm paralyzed by the phrenic nerve operation prior to the establishment of the second pneumothorax—in one a 90 per cent pneumothorax plus the diaphragmatic paralysis on one side and a 20 per cent collapse on the other, in the second, a 40 per cent collapse on one side and a 30 per cent pneumothorax collapse plus diaphragmatic paralysis on the opposite side. In each, the phrenic nerve operation was done on the primarily involved side, while the patient was still on unilateral pneumothorax.

One patient included in this series had the second pneumothorax established during the sixth month of pregnancy because of contralateral extension of the disease with pulmonary hemorrhage. Her progress was uneventful until approximately 1 week before the calculated date of delivery, when a small pulmonary hemorrhage occurred from the second side, which could not be controlled by increasing the pneumothorax. She was delivered of a living child by Cesarean section performed under spinal anesthesia without difficulty and was alive and in good condition 3 years later. Two cases have undergone operations for acute appendicitis under spinal and one under local infiltration. No difficulties have been encountered during the operation or subsequently. [We believe spinal anesthesia inadvisable under any of the above circumstances. EDITOR.]

In the group reported by Mattill and Kinsella (*Ibid*), 90 have actually received bilateral pneumothorax to a greater or less degree—the treatment of 35 may be considered to have been clinically successful in that it controlled the tuberculosis, closed cavities, and rendered the sputum negative; 23 may be listed as partially successful, benefiting the patient to a considerable degree, reducing but not completely closing all cavities, while leaving the patient with some sputum, usually negative, but occasionally containing tubercle bacilli. Three of more recent date must be listed as questionable, and 29 as failures, because of inability to collapse cavity, control tuberculosis or render the sputum negative. Of these, 25 are now dead, 3 still in a sanatorium, 1 alive and in good condition.

The group of patients upon whom bilateral pneumothorax was attempted unsuccessfully presents a picture which is quite discouraging except for a few individuals upon whom some other type of collapse has been substituted for the attempted bilateral pneumothorax. Eleven are dead, 7 others in whom no other collapse was possible presenting an unfavorable or very questionable prognosis.

COMPLICATIONS—The complications encountered in the group observed by Mattill and Kinsella (*Ibid*) have been enumerated as (1) accidental pneumothorax; (2) spontaneous pneumothorax; (3) over collapse of the lung; (4) mediastinal hernia; (5) pleural effusion; and (6) purulent effusion.

Noteworthy in the group of *hernia*, recognized in 14 of the cases, is one that progressed from right to left to such a degree that it performed an almost complete extrapleural pneumolysis on the left side. Eventually, air was injected into the right pleural cavity and its hernial extension through needle puncture sites in both axillary regions.

*Effusions*—The development of effusions during the course of pneumothorax therapy is a recognized drawback and danger, and thoughtful consideration of the predisposing factors and methods for the reduction of its incidence are advanced. A. A. Pisani and F. J. Smejkal (*Tubercle* 15: 216 (Feb.) 1934) state that, according to most authorities, it is to be expected in about 50 per cent of cases followed through from start to finish. P. Starcke (*Ztschr. f. Tuberk.* 70: 401 (July) 1934) quotes 2 sets of statistics, one giving an instance of 50 per cent, the other of 68 per cent and, again, Mattill and Kinsella (*loc. cit.*) in their series of cases of simultaneous bilateral pneumothorax apparently had a total of 50 instances of effusion in a group of 90 patients in whom the gas therapy was possible, approximately 55 per cent. M. Joannides (*Am. Rev. Tuberc.* 29: 313 (Mar.) 1934), however, makes the startling statement that the incidence of pleural effusion in 5610 pneumothorax injections was “only 27 cases of pleural effusion, 10 of which developed on the right and 17 on the left.”

That this complication does not necessarily add greatly to the ultimate disease mortality is shown by the final figures of Mattill and Kinsella (*loc. cit.*) its prevention is exceedingly desirable in that it entails a reduction in the worry and labor of the continued treatment. A distinct disadvantage is the sequence of an adhesive pleuritis, causing a partial loss of pulmonary collapse, which may at times be answered by an oleothorax. The great danger of it lies in the possible development into a purulent effusion, whether tuberculous or nontuberculous. Of 12 cases presenting complication of purulent effusion in Mattill and Kinsella's

series, 11 had previously had clear effusions, and in 2 of the group a secondary infection had been superadded.

Pleural effusion met with in pneumothorax treatment, according to Pisani and Smejkal (*loc. cit.*) is *due* to: (1) an increased permeability of the capillaries, because of oxygen lack; (2) increased osmosis; (3) higher concentration of H ions; (4) calcium deficiency of the pleura; and (5) the aspirating effect of the endopleural negative pressure. To these primary causes, may be added another important factor, although contributory in nature, *viz.*, any condition which causes a sudden drop in blood-pressure, as, for example colds, overexertion, psychic depression, influenza, etc.

This problem, in its *causation* particularly, is viewed from another angle by M. Joannides (*loc. cit.*) the material being taken largely from the Chicago Municipal Tuberculosis Sanitarium. He states that the etiological factors of effusion may be either infectious, mechanical or chemical. Infection may be introduced from air that is injected into the pleural cavity and, more frequently, through improper manipulation of the point of injection, or imperfect technic in the insertion of the needle. It has been customary for physicians who do thoracentesis to localize with the tip of their finger the intercostal space at the point of insertion of the needle. This is quite the proper technic if perfectly sterilized gloves are worn and strict operating room technic followed; however, needle insertions are usually made without gloves, and in spite of careful chemical and mechanical cleansing of the hands, pathogenic bacteria are bound to remain at the tips of the fingers and are implanted on the skin of the patient, and may be introduced along with the needle into the pleural cavity, thus causing infection. To prevent this, it has been customary for the writer to insert the needle into the subcutaneous tissue first, and then localize the intercostal space at a point slightly above the site of the skin insertion, so that neither the skin nor the needle may come in contact with the operator's hand.

In the *prevention* of pleural effusion Pisani and Smejkal (*loc. cit.*) use **calcium gluconate** because of its ease of administration and lack of local irritation. The drug was injected intramuscularly in the gluteal area in 10 c.c. amounts of 10 per cent concentration, 3 times weekly for 2 months, twice weekly for 2 months and then weekly during the continuation of the treatment. In later months of their work, the drug was administered orally 2 hours after meals, *tertio id.* as well. It has been impossible as yet to draw conclusions as to the value of this later additional procedure.

The *results* reported are as follows. The 34 patients, observed for a period of about 14 months were all advanced cases, and with the exception of a few, all exhibited marked adhesions—these are the very ones who are more prone to develop pleural effusions. Of this group of 34, twenty received calcium injections, and 14, the control group, did not. Both groups were otherwise treated in an identical manner. Among the 20 treated with calcium gluconate, only 2 effusions have been observed, and in both a small collection of fluid could be seen in the costophrenic sinus. Two negative patients were given gas for but a short period, so should be excluded. Among 14 patients of the control group,

the effusion was noted 7 times, which, in contradistinction to those of the preceding group, were rather copious

A comparison with the figures of the institution revealed to Pisani and Smejkal (*loc cit*) that between 1925 and 1929 the percentage of effusions was 45, and from that time to the present, it is 23.9 per cent. compared to 11.1 per cent. in their treated group

The conclusions reached by Joannides (*loc. cit.*) are as follows: Pleurisy with effusion is quite a common sequel in collapse therapy by artificial pneumothorax. It is not dangerous in itself unless secondary infection is introduced or effusion results from an infection introduced either through the lung or from the outside. The number of cases with pleural effusions may be diminished by a careful and rigid observance of the rules of asepsis during the insertion of the needle, and by the injection of uncontaminated air into the pleural cavity. It is felt advisable to aspirate definite amounts of fluid and introduce air in order to maintain a hydropneumothorax, so that if at any time the effusion becomes rapidly absorbed, it will prevent the formation of pleuropulmonary symphyses

**Phrenic Nerve Operations.**—With perfection of other methods of collapse therapy, especially the upper selective thoracoplasty, more critical attention is being given to the indications for, and the end-results of phrenic nerve interruption. Phrenic nerve interruption as the sole surgical measure of collapse therapy holds less favor than it did but a few years ago, and in those instances of upper lobe disease where its *adjuvant* help is deemed of value, the added immobilization from section of the scalene muscles at the time of the phrenic nerve operation is recommended

The technic of the procedure is so well established as to need no consideration, but help to the clarification of the indications for and contraindications to its performance are in order

In discussing the *results* of phrenic nerve operations, A. V. S. Lambert [Thoracic Surg. 4: 49 (Oct.) 1934] states that it is well in considering indications and contraindications for the operation to summarize what occurs following interruption along the phrenic nerve pathway. One-half the diaphragm is paralyzed and eventually its muscular fibers atrophy and are replaced by fibrous tissue. This is complete and confined to one-half of the diaphragm. A paralyzed diaphragm is more or less flaccid, and its movement is dependent on the intrapulmonary and intraabdominal forces which act upon it. The resultant of these forces will determine its eventual stationary position. Coincident to this change in position, the size of the superimposed lung is diminished and the tension of its tissues is in some measure relaxed

The elimination of the phrenic nerve pathway abrogates an important link in the coordinating mechanism between the various factors entering into the function of breathing, in that during the respiratory cycle the intercostal and abdominal muscles act less vigorously. This, together with loss of contractile power in the diaphragm effects a certain degree of rest in the pulmonary tissues.

Graham and others have demonstrated that following diaphragm paralysis the effectiveness of cough in expelling lipiodol introduced into the lung is interfered with in that the elimination of iodized oil from the lung is retarded and that

on some occasions coughing may actually drive material such as lipiodol more deeply into the lung. It is realized that there is a wide divergence of opinion among equally conscientious observers in respect to the influence which diaphragm paralysis has on cough, but in view of the writer's experience and the testimony of others, the possibility of such interference should be reckoned with and in the presence of profuse expectoration, the clinician should pause and consider the advisability of recommending a phrenic operation no matter what may be the nature of the pulmonary lesion.

A considerable number of patients have come under observation at Bellevue Hospital, previously subjected to phrenic nerve operation, who present large cavities having their walls firmly adherent to the parietes and virtually occupying the entire apex of the thorax. The dangers and evil consequences due to the loss of effectiveness of coughing are frequently seen in such cases, where the secretion is abundant and the dangers of bronchogenic spread into the lower lobe are enhanced. A phrenic nerve operation should not be performed on such patients, even if it is the only procedure to which the patient will consent.

A second group of patients have been observed with an extensive chronic diffuse fibroid or fibrocaseous lesion. Here, the chances of benefit following the operation are small indeed. The disease process has largely replaced the elastic tissue in the lung by dense fibrosis; the diaphragm is often a firm immobile structure; and the operation accomplishes nothing.

The operation at present is performed most frequently as an aid in the closure of cavities. Here the greatest amount of judgment is required. Cavities should be judged from 2 standpoints: (1) their exact site, and (2) the nature and the extent of the surrounding tissues. The author classifies cavities as central and peripheral. The *centrally located cavities* are those completely surrounded by more or less normal lung, and the *peripherally located cavities* are those which have more or less of their walls adherent to the parietes of the chest. The latter relationship jeopardizes the chances of a successful result in proportion to the extent of the adhesion.

The nature and extent of the lesion surrounding the cavity are, however, the most important factors in estimating the chances of success to be derived from the operation. The most favorable cases are those presenting cavities centrally located, surrounded by zones of young, soft, fibrous tissue, and which are comparatively well stabilized, as evidenced by no fever or toxemia. Whether the lesion is situated in the upper, middle or lower part of the thorax does not seem to influence the prognosis.

The use of the *phrenic operation as a preliminary step to thoracoplasty* is still a matter of dispute, according to Lambert (*Ibid*). Although it has strong adherents, the writer's experience has led him to abandon its use as a routine procedure, and today he employs it only in those cases in which it may serve as an aid in stabilizing the lesion. The possibilities of interfering with the effectiveness of the act of coughing and, in consequence, increasing the dangers of a bronchogenic spread, outweigh the advantages in lesions which are in themselves not favorable for phrenic operation. Prolonged bed rest in these cases has proved a safer procedure.

Lambert (*Ibid.*) further states that he has always believed that the first stage of a thoracoplasty should begin with the upper ribs and has found that the cases which have undergone a preliminary phrenic operation have had a stormier course. The lower portions of the lung become suffused with secretion, as shown by diffuse density on x-ray examination during the first few days following operation. These patients run a febrile course at times sufficiently elevated to be alarming, and they have greater difficulty in raising the secretion by coughing.

In addition, it has been found that the rise of the diaphragm, with the consequent rise of the intraabdominal organs, has been a real obstacle in effecting a satisfactory collapse of the lower and middle region of the lung in the subsequent and later stages of thoracoplasty because the abdominal pressure tends to hold outward the chest wall from which the lower ribs have been removed. The writer also believes that an active diaphragm, by its inherent muscular tonus and contraction, will pull inward the anterior ends of the resected lower ribs and will also aid the action of gravity in drawing inward the upper chest wall after removal of its support of the upper ribs by maintaining a constant downward traction on the pulmonary tissue, and will thus aid collapse.

*Late Untoward Results of Phrenicectomy*—A rather startling autopsy report of 11 cases, upon whom phrenicectomy as a single or as one of a group of surgical measures had been performed at intervals varying from 3 weeks to 6 years is made by W. S. Stanbury (*Am Rev Tuberc* 29: 528 (May) 1934). After detailing the gross and microscopic evidence of atrophy already evident in the specimen obtained only 3 weeks after the operation and so complete in the other 10 that "through this thin translucent membrane the underlying organs could be seen distinctly" he goes on to recording the form and position of the abdominal viscera.

Ten of the 11 cases of Stanbury's series showed definite morphological abnormalities of the abdominal viscera. In both cases of left phrenic paralysis the stomach occupied a vertical position in the left upper quadrant. The cardiac portion was displaced upward and was dilated. The greater curvature was directed forward, the duodenum was displaced to the left. In case 5 the stomach was tremendously dilated. In its upper two-thirds the greater curvature pointed laterally and in its lower third posteriorly, producing a constriction across the anterior surface of the stomach. Both loculi so formed were ballooned out and tense. The duodenum was markedly dilated for a distance of 7 cm. beyond the pylorus.

In the 8 cases of right phrenic paralysis (9 examined) the longitudinal axis of the stomach tended to be transversely. Two stomachs presented a uniform constriction in their midportions, giving the organ an hour-glass appearance. In 3 cases the stomach was tremendously dilated. The gastric wall was thin and the rugæ were ironed-out. The superior mesenteric artery was pulled tightly over the duodeno-jejunal junction and the bowel distal to it was collapsed.

As stated already, 4 cases of the series died not as the result of their tuberculous disease but of gastroduodenal ileus. In none were any of the well-recognized causes of obstruction demonstrable at necropsy. In 1 case only was the diagnosis

made clinically. In 2 the continued abdominal discomfort was thought to be due to tuberculous enteritis, but such involvement was found in neither.

The following conclusions are reached by Stanbury:

"Whether section of the phrenic nerve and the resulting paralysis of the diaphragm bear a causal relationship to acute upper intestinal obstructions, such as reported by Bonafé and Poulain (*Presse méd.* 40: 1104 (July 13) 1932) and described by the writer in the present communication, must await further investigation.

"In view of the marked distortion of the abdominal viscera in 10 of the 11 cases, 3 of which had fatal gastroduodenal obstruction, the possibility of such complications must be considered seriously when advising phrenicectomy for the treatment of pulmonary disease."

PHRENIC NERVE OPERATION AND SCALENIOTOMY OR SCALENIOTOMY AND PHRENIC NERVE OPERATION COMBINED.—L. Fisher (*J Thoracic Surg* 4: 41 (Oct.) 1934) discusses the subject of scaleniotomy with, or subsequent to, phrenicectomy in the treatment of pulmonary tuberculosis and reports the analysis of a series of 135 cases in which this combination of procedures was done. He states that the ideal lesion in which to expect response to scaleniotomy is one situated above the anterior level of the second rib; even in this location cavities should be preferably not more than 4 cm. in diameter and relatively thin-walled. If cavity is present, there should be sufficient elastic lung tissue surrounding it on all sides to permit enough resilience for fibrotic contraction. Cavities which are subpleural offer less hope of closure by simple pulmonary relaxation. In those patients who show decided elevation of the upper ribs on normal inspiration, scalene section offers greatest relaxation to an adherent lung apex.

In discussing the evidence of limitation of respiratory excursion by this procedure, the following rather surprising statement is made: "In one patient, who had bilateral scaleniotomy without phrenicectomy, the vital capacity was permanently reduced 350 c.c. or 14.9 per cent. In a human subject, immediately after death, Aycock found experimentally that a 40 per cent decrease in apical volume was produced by section of the scalene muscles."

*Technic*—The technic as indicated is simple. It is done through the customary phrenic incision, slightly above and parallel to the clavicle, under local anesthesia. Injury to the internal jugular vein or subclavian artery, or to the inferior trunk of the brachial plexus, constitutes the chief source of danger. When prior phrenicectomy has not been done, the phrenic nerve is blocked, clamped and severed close to its origin. Accessory phrenic nerve roots are resected. Evulsion of the main stem is reserved until after scalene section, because exsanguination elicits the chief discomfort of the combined operation. The scalenus anticus is dissected free from the carotid sheath and brachial plexus, hooked up with a straight aneurysm needle as close as possible to its insertion, and severed by low heat galvanocautery, which provides hemostasis. The side walls of the rather deep wound should be protected against heat radiation by wet saline packs. The plexus can then be retracted medially, and the scalenus medius dissected out and divided.

Caution must be taken to preserve the long thoracic nerve, which is usually found within the posterior sheath of the medius, but occasionally traverses the belly of the muscle. The dorsal scapular nerve is usually encountered also. The scalenus posticus is then simultaneously divided. The muscles being insensitive, pain may be produced only by dissection or



retraction of the brachial plexus and its branches. A slight transitory anesthesia or paresis in the arm or hand may be produced, but rapidly disappeared. No deformity or loss of function can be noted.

Thirty-four cavities were closed by scaleniotomy, with or subject to phrenicectomy. The majority closed were cavities having a diameter of 2 to 4 cm. "Honey comb" cavities proved definitely refractory to closure. By scaleniotomy, with or subsequent to phrenicectomy, 50.6 per cent were rendered bacillus-free.

In 37 cases of the series the scaleniotomy was done anywhere from 6 months to 3 years subsequent to phrenicectomy. All of these patients had more than 6 months of bed rest; in practically all, pneumothorax had been found impossible or else unsatisfactory, due to apical adhesions. In this group, 31 per cent cavities were closed and in 42.9 per cent the sputum was rendered bacillus free by this measure.

**Thoracoplasty.**—In the combined series of cases collected from American and Continental sources, covered in the paper of Hedblom and Van Hazel (*loc. cit.*), the very large group there considered consisted in overwhelming proportion of well-advanced cases in whom the complete posterior thoracoplasty procedure, the Sauerbruch or Brauer technics, and various modifications, had been necessary. With increasing study of the thoracoplasty problem, and the more widespread appreciation of its benefits, the indications for this procedure are being recognized earlier in the course of the disease, at a time when the very extensive work, with its attendant shock and severe postoperative strain will not be necessary, and when the patient, less reduced by chronic intoxication, will have increased chance for operative recovery together with the conservation of a considerable amount of now uninvolved but otherwise ultimately doomed lung.

Various terms have been applied to the procedure, *i. e.*, selective thoracoplasty, upper stage thoracoplasty, superior thoracoplasty, etc., indicating its limited extent as compared with the originally advocated thoracoplasty procedure. Of greatest importance has been the recognition of the fact that with the limitation of the need of an extensive area of rib resection, and the early use of this procedure in unilateral involvement, there has been an extension of the field of possible usefulness to the cases of bilateral upper lobe tuberculosis where pneumothorax therapy may, for intrinsic or extrinsic factors, be unsuitable or impossible.

Indicative of the advances that have been made in the technic of operation, may be mentioned the reports of O'Brien who, in a discussion of a paper by P. W. Coryllos on thoracoplasty *versus* pneumothorax (*J. Thoracic Surg.* 4:30 (Oct.) 1934) says, with reference to patients in whom only the 3 upper ribs were removed: "I might add that the mortality rate in this group last year was 1.6 per cent. It is now up to 2.6 per cent. This from a group of 151 patients." On the same subject, Coryllos (*loc. cit.*) reported in the same discussion that apical thoracoplasty in apical lesions gave 70 per cent clinical cures and only 2.3 per cent mortality.

H. Jessen (*J. Thoracic Surg.* 4:1 (Oct.) 1934), discussing thoracoplasty in bilateral cavernous tuberculosis, evaluates the situation in the following words: "One of the greatest advantages of partial thoracoplasty seems to me to be the

fact that it takes good care of the heart as well as of the mediastinum. Therefore there is practically no shock after the operation; and, if it affects the heart to a certain degree, this affection is slight, and of only temporary significance. It can be said that *superior thoracoplasty* today is an operation without any risk and danger, because the mediastinal organs are not greatly injured. Consequently the mortality has become very low or even zero . . . Especially does thoracoplasty include still further possibilities of bilateral treatment, and I feel certain that the perfection of partial thoracoplasty will some day convince those still in doubt. . . . Considering now the exact indications for partial thoracoplasty, especially for the bilateral operation, we find another great advantage in that it eliminates only affected tissues and saves all the healthy parts of the lung."

INDICATIONS.—Coryllos (*loc. cit.*), under indications for thoracoplasty, has the following to say about this important phase:

"In the routine work of our medicosurgical conferences, our group has endeavored to answer the following questions: (1) What are the cases which should be operated upon; (2) when should they be operated; (3) how should they be operated?

"These indications are far from being always easily answered. We have arrived, however, at a number of conclusions upon which our present conceptions of operative indications are based.

*What are the cases to be operated upon?* (Choice of cases). The answer to this question is not based upon the duration of the disease, its location, extension, or upon the general condition of the patient. It is principally, and may be said exclusively, based on the nature of the disease. The distinction of the acute from the chronic forms of pulmonary tuberculosis, and the separation of the latter into resolving forms, which can be considered as benign, and into caseous pneumonic or ulcerating forms, which should be considered as the malignant forms of the disease, have thrown, the writer believes, a new light on the question of operative indications. The chronic proliferative or productive forms have come to be considered as nonsurgical, provided that no cavities are present. Surgical as well as medical treatment has very little, if any, influence upon these slowly progressive, often ignored, and, as a rule, perfectly well tolerated lesions. This fact is of importance because a number of the so-called "good risks" for thoracoplasty belong to this class; it is questionable whether their "cure" by surgical procedures can be attributed to the operation. According to the writer, this is shown by the fact that a great number of his cases with caseous pneumonic tuberculosis on one side, and chronic productive on the other, although operated on only on the side of the caseous pneumonic lesion, were cured and behaved as unilateral cases.

The *acute exudative resolving forms* do not require surgical treatment any more than do the productive forms. As a rule, they recover spontaneously under simple bed rest within a few weeks to a few months. The whole question of operative indications thus evolves around the accurate diagnosis of the form of tuberculosis which is being dealt with. This diagnosis is difficult, if not impossible, at the acute phase of the disease. A benign exudative form can be suspected, however, by its lesser toxicity, better general condition of the patient,

smaller numbers of bacilli in the sputum, and the fewer stethoscopic signs, considering the radiographic extent of the disease; it is the opposite in the caseous ulcerative forms. Within 5 to 15 weeks the diagnosis becomes easy, since at this time the benign forms show a more or less advanced resolution; whereas in the caseous pneumonic forms cavities appear following the elimination of the sloughed-out pulmonary tissue.

It has often been said that this classification is not reliable because there is no such thing as an exclusively resolving form or an exclusively ulcerating form of tuberculosis. Clinically, however, predominance of one of these two forms is usually so marked that they may be considered for surgical purpose as pure forms, with the restriction that whenever even a small cavity is present, the exudative element should be disregarded and the case should be diagnosed as caseous pneumonic and ulcerative form.

It is thus evident that before any surgical treatment is decided upon, time should be allowed for an accurate diagnosis of the form of tuberculosis of the individual case which is being dealt with.

On the contrary, when the presence of a real cavity has been ascertained, the writer believes that no time should be wasted. He considers that a patient who has a tuberculous cavity and highly positive sputum must have the lung collapsed without delay unless there are definite and imperative contraindications. Such a patient should be placed in the same category with patients who have a tuberculous kidney. As in this, operation should be done before the disease becomes unmanageable. The writer does not believe that hemoptysis, tuberculous laryngitis, or even a moderately advanced tuberculous enteritis constitute contraindications. The only way to cure these complications is to collapse the diseased lung and eliminate the source of tubercle bacilli.

The questions become more difficult when bilateral lesions are considered. Coryllos and his associates have arrived at the following conclusions on this question:

"With cavities in one lung and lesions in the other lung of the chronic productive variety, unless the latter are so extensive as to very markedly decrease the respiratory field, there is no contraindication to thoracoplastic collapse of the caseous pneumonic side. When cavities are present in both lungs, the operability of the patient depends upon their extension and chiefly upon their location. In bilateral apical lesions we should collapse both apices. When apical lesions are present in one lung and extended lesions in the other and the condition of the patient is not too desperate, we collapse the apex which shows the more advanced lesions, leaving to a later date the procedure to be applied upon the other lung, pneumothorax, apicolysis or thoracoplasty."

"*When should we operate?*"—Since we know that cavities even small in size, if left uncollapsed, constitute a death sentence in 80 per cent of patients, that thick-walled large cavities develop from the small cavities; that small cavities are easy to collapse; that no harm can be caused by a timely collapse even to the fortunate 10 to 20 per cent who may cure spontaneously and that there are no means by which we can foretell whether a given cavity is going to cure spon-

taneously or not, for all these reasons we are not justified in delaying collapse treatment."

"*How shall we operate?*—When the cavities are exclusively located in the apex of one lung, the method of choice is **apical thoracoplasty**. It does not matter what the size, character of the walls or number of the cavities may be, provided that we are certain that true cavities are present.

"In bilateral but exclusively apical lesions, the method of choice is **bilateral apical thoracoplasty** if the condition of the patient is fair and he does not have frequent hemoptysis. In the latter cases, it is preferable to first perform a **temporary apicolysis** with plombe upon the more advanced side and from 1 to 3 weeks later proceed with an **apical thoracoplasty** on the other side; in this way we may avoid the danger of a hemoptysis from the contralateral and as yet uncollapsed side, following apical thoracoplasty. Apicolysis, although less effective than thoracoplasty, is a much more benign operation and permits the performance of a thoracoplasty on the other side, with less danger of a fatal hemoptysis. Apicolysis, as shown in my cases, can be trusted to control hemoptysis. A secondary thoracoplasty, if necessary, may be performed at a later date on the side on which apicolysis was done.

"When the cavities are situated lower than the third rib, **pneumothorax** is a better procedure. Although the percentage of cures obtained with thoracoplasty is higher than with pneumothorax, the early and late mortality of extensive thoracoplasties and the deformities left by it demand a serious previous trial of pneumothorax. In cases of failure of pneumothorax to collapse the cavity because of the presence of adhesions, **closed pneumolysis** should be used. If this method also does not produce a satisfactory collapse of the cavities, **thoracoplasty** must be decided upon without further delay."

**Apicolysis (*Extrapleural Pneumolysis with Paraffin Pack*).**—Experience has not been sufficient, to date, to indicate positively the best procedure in surgical therapy of tuberculosis of the lung apex.

P. N. Coryllos (J Thoracic Surg 4 30 (Oct) 1934) records his results and favors a complete *upper thoracoplasty*. Other operators refer to the same procedure as a *selective thoracoplasty*. H. Neuhoef (Ibid 3 270 (Feb) 1934) proposes a much more radical procedure, advocating the gradual reduction of the thickness of the dense wall of the cavity at the time of operation to assure its collapse. Again, the use of the *extrapleural pack* is advocated by J. R. Head (Surg Gynec Obst 59 215 (Aug) 1934).

It is evident from this diversity in the opinions of those who are giving thought to work of this kind, that many factors, involving the economic status of the patient, extent of pathology, the operator, and equipment, must be given consideration in planning the procedure in a given case.

The number of methods devised for the obliteration of apical cavities is numerous. The best results will be obtained by the surgeon having the greatest number of procedures at his command, and who, at the same time, by his thorough knowledge of the case in hand, can select and carry forward the technic best suited to the individual's requirements.

The *indications* in the individual case must take into consideration the general condition of the patient, whether the process is unilateral or bilateral, the extent of the apical lesion, especially in relation to the level of the clavicle, and the position of the cavities, whether nearer the anterior or posterior thoracic walls.

**EXTRAPLEURAL PACK**—J. R. Head (*loc cit.*) reports on 28 personal cases in which the extrapleural pack was used and concludes that (1) the operation has such narrow indications that, for most, the accumulation of a larger group would require many years, and (2) whereas in Europe the procedure has been used since 1912 and is gaining rapidly in popularity, in this country most have rejected it without trial on the basis that it is unsurgical.

*Indications*.—1. Productive unilateral and bilateral apical lesions with single or multiple small cavities which do not extend below the fourth or fifth ribs at the spine, and in which there is no active or progressing disease, and no disease in the remainder of the lung

2. Large cavities and more extensive lesions in cases in which the age or condition of the patient, or disease in the opposite lung contraindicate thoracoplasty.

3. Cavities which have remained open after complete thoracoplasty.

4. Hemorrhage from apical cavities which cannot otherwise be controlled

In discussing these indications, Head says that "the first is the only one that has been disputed. Many have held that when thoracoplasty was feasible, the operation should never be used," and cites Sauerbruch as having earlier held to this opinion, but as having now adopted it as the operation of choice for small apical cavities, and himself describes the procedure as simpler, safer, and less deforming than thoracoplasty, and is the only method of collapsing diseased, without sacrificing normal, lung

*Technic*—The posterior approach is advocated on the basis of affording a better access to the apex, and, therefore, a more satisfactory collapse, and on the basis of his own personal end-results. He believes that the use of instruments in effecting the separation in the extrapleural plane is dangerous, because of increasing the risk of lung injury, saying that if dissection of the plane with the finger is not easily accomplished, it should be abandoned.

The formula of the paraffin pack used is that originally suggested by Baer

Paraffin, melting point 48-50, 100.0 Gm

Iodoform, 2 Gm

Bismuth carb. neutral, 10 Gm

*Postoperative complications* (early)

(a) *Infection*—Usually requires removal of paraffin

(b) *Emphysema*—Occurs immediately in cases in which lung has been injured. Opening is required if pressure symptoms develop

(c) *Serous effusion*—Probably always present in limited amount. It should be aspirated only if it is copious, is causing symptoms, or seems to threaten an extrusion of the pack

(d) *Pressure on heart and vessels*—Unusual and has occurred only where large masses have been put in under pressure

(e) *Aspiration*—Here, as in other operative procedures, atelectasis and aspiration pneumonia are most likely where there is copious sputum and the diseased lung soft. Preoperative expulsion of sputum by cough and postoperative postural drainage and withholding of opiates, will aid in the reduction of these dangers

(f) *Tuberculinization*—An immediate severe intoxication has been reported Coryllos (*loc. cit.*), in his article on thoracoplasty, has spoken of it as tuberculin shock. The suggestive signs are immediate severe prostration, vomiting, high fever with small, rapid pulse and low blood-pressure.

*Postoperative complications (late):*

(a) *Extrusion of paraffin*.—This may take place weeks or months after operation. Healing usually promptly follows removal of the remaining paraffin and in some instances the compression of the pack has served its purpose in securing healing before its extrusion.

*Results*—R. B. McIndoe and J. Alexander (*Am. Rev. Tuberc.* 29:270 (Mar.) 1934), as an introduction to their article, state that for years they were opposed to the use of extrapleural pneumolysis with paraffin filling because it is contrary to accepted surgical practice to place a foreign body permanently in the tissues. The fact that they were frequently seeing patients with cavernous phthisis for whom all other probably effectively collapse therapy procedures were contraindicated, the great majority of whom would probably die from tuberculosis if not aided by surgery, finally compelled them to adopt the operation in spite of its defects.

Pneumothorax was attempted in all but one patient who, having been in a sanatorium for several years, requested that a paraffin pneumolysis be used in preference to pneumothorax. In only 4 patients was any pneumothorax whatever obtained; in them it was wholly unsatisfactory, and there was no indication for intrapleural pneumolysis.

Before operation all of the patients had open cavities and tubercle bacilli in the sputum, and the majority had active bilateral tuberculosis. The last report of the writers shows that 69.9 per cent. were arrested, apparently arrested, quiescent or improved, and 30.1 per cent. were unimproved or dead.

In a summary of the thoroughly studied group of 42 cases made by McIndoe and Alexander (*Ibid.*), they state that although long prejudiced against introducing a foreign body permanently into the tissues, 2 years ago they began to use paraffin pneumolysis for patients whose prognosis was hopeless if this operation were not used.

In the past 2 years they have employed it 42 times. In 3 patients a thoracoplasty might safely have been used in its place. In 3 others, very recent active tuberculosis in the contralateral lung made thoracoplasty of greater than average risk. In 37 patients thoracoplasty was definitely contraindicated, chiefly because of extensive bilateral tuberculosis.

The tuberculosis in 69.9 per cent. of the patients has been arrested or improved and 30.1 per cent. are unimproved or dead. Six of the patients, whose disease did not become arrested, subsequently had a thoracoplasty, and 4 of them are practically well, 1 is greatly improved and 1 is dead.

In the 29 cases in which extrapleural adhesions did not prevent the surgical formation of an adequate extrapleural space to receive the optimal amount of paraffin, 68.9 per cent. of the cavities became closed, whereas, in the 14 cases in which the extrapleural cleavage was unsatisfactory, only 7.1 per cent. of the cavities were closed.

The results in those cases in which the posterior approach was used are superior to those in which the anterior approach was used. Extrapleural cleavage was satisfactory in 89.5 per cent of the posterior operations and in only 50 per cent. of the anterior operations.

Among the patients with satisfactory cleavage, the cavities became closed in 76.5 per cent. of the cases that had had the posterior operations and in 58.4 per cent. in those having had the anterior operation.

Although paraffin pneumonolysis is a less effective operation than a properly performed thoracoplasty and is subject to several complications, McIndoe and Alexander have found that it produces many perfect results, and is virtually indispensable for certain cases in which all other therapeutic measures that might be expected to arrest the tuberculosis have been tried or are contraindicated.

**SUPRAPERIOSTEAL AND SUBCOSTAL PNEUMOLYSIS WITH FILLING OF PECTORAL MUSCLES**—In the small number of cases where the cavitation process does not rise above the level of the clavicle, nor descend below the level of the third rib, and where the vomicae lie nearer the anterior than the posterior thoracic walls, J. Alexander (Arch Surg 28: 538 (Mar.) 1934) has suggested a modification of the apicolysis procedure which he calls a suprapariosteal, and subcostal pneumolysis with filling of pectoral muscles.

The *advantages* claimed are the following:

1. Use of an endogenous, vascularized and innervated filling material, whose shrinkage is slower and disorganization less likely than that of a free graft.
2. In the suprapariosteal approach the pocket is further removed from the seat of actual pathology than where an extrapleural apicolysis is done, and therefore infection less likely.
3. The creation of the pocket is technically less difficult because the internal periosteal layer is not opened, the pleura never exposed. The operation may therefore be used in the presence of partial pneumothorax.
4. As no rib is resected, the filling is efficiently retained and the expectorating mechanism, which is important in the prevention of stasis pneumonia, is but little interfered with.
5. The periosteum of the bared ribs is pushed deep into the thorax and presumably forms new ribs within approximately 6 weeks, which tend to maintain the lung in the collapsed position even though the muscle atrophies.

The operative *technic* is clearly indicated by Figs. 1, 2, 3 and 4.

One of the chief *limitations* is that it is indicated only for cavities that do not extend above the clavicle, because separation of the lung and pleuræ, together with a protecting layer of soft tissues, is not possible above the superior edge of the first rib.

The sudden reduction in volume of the diseased lung causes secretions to flood the bronchi and it is therefore important that the patient expectorate as completely as possible as soon as he awakens on the operating table from the gas anesthesia and that he continue to expectorate freely during the post-operative period. Immediately before operation he should have coughed up all loose sputum.

**Cavernolysis.**—To some, the end-results of thoracoplasty have not been as satisfactory as they would desire, the mortality and morbidity of operation have proved higher than it is felt should obtain and end-results, as gauged by complete closure of cavities and persistently negative sputum, have not met their

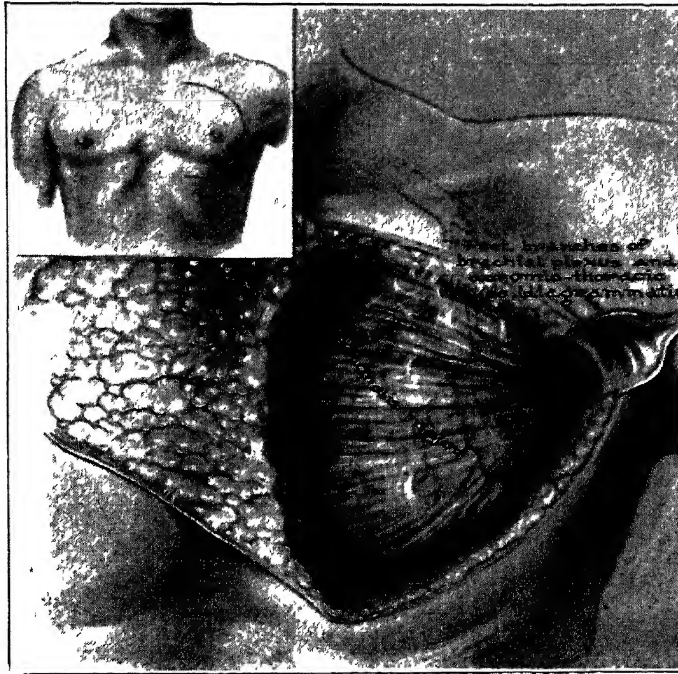


Fig 1—Cutaneous incision. Position of chief nerves and vessels (acromioclavicular axis) of pectoral muscles indicated (J Alexander Arch Surg)

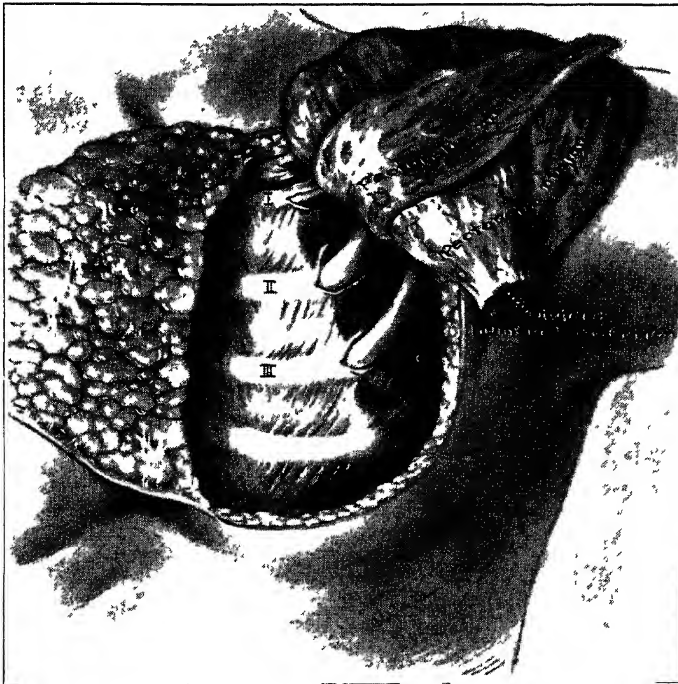


Fig 2—All of pectoralis major, except its clavicular fibers, detached from thoracic wall and humerus. Pectoralis minor detached from ribs but not from coracoid process. Chief neurovascular pedicle of both muscles intact. Parts of upper 3 ribs freed from periosteum. Periosteum, intercostal muscles and underlying lung retracted from bare ribs (J Alexander Arch Surg)



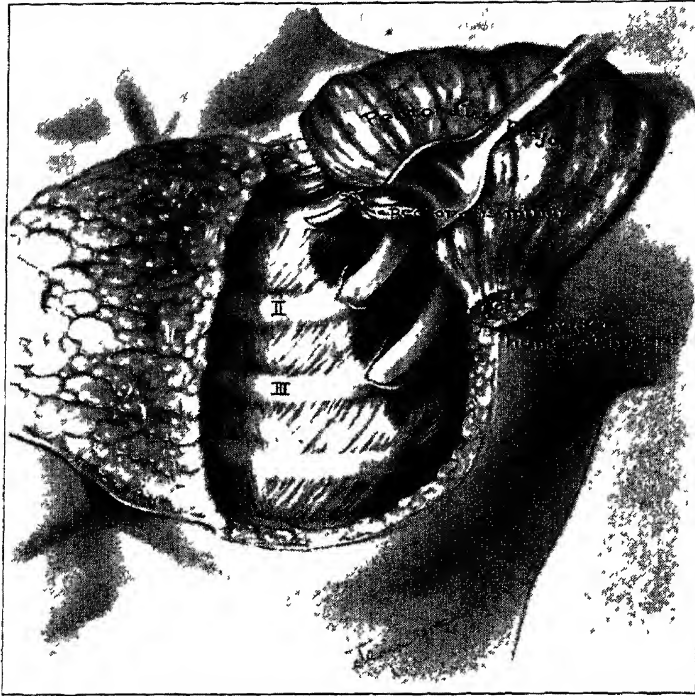


Fig 3 —Pectoralis minor tucked into first intercostal space and tacked in place under first rib (J Alexander Arch Surg)

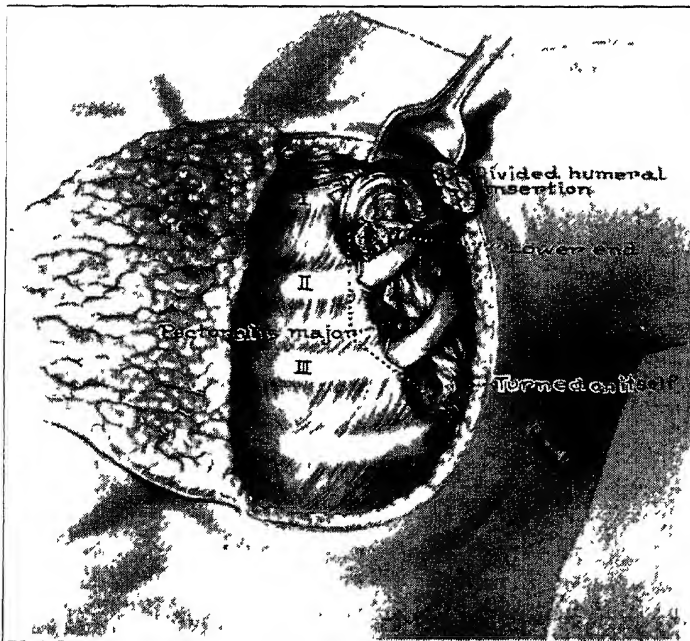


Fig 4 —Pectoralis major pulled through first intercostal space, downward beneath second and third ribs and out through third intercostal space. Its deep surface then stitched to periosteum of fourth rib and redundant muscle pulled upward beneath third and second ribs and stitched to itself in first intercostal space. Drain for serum placed independently in axilla (J Alexander Arch Surg)

expectations. Because of such primarily unsatisfying end-results, the anterior extension of the rib removal has been advocated to the costochondral junction, with removal of part of the cartilages themselves, as done by Coryllos (*loc. cit.*); and in cases where the older type primary operation has not produced complete cavity obliteration, an additional anterolateral thoracoplasty is advised.

H. Neuhof (J. Thoracic Surg. 3:270 (Feb.) 1934) in the exploration of the lesion and pneumocavernolysis in the operative treatment of pulmonary tuberculosis is advocating a radically different addition to the usually performed thoracoplasty procedure. The main purpose of this presentation, according to the author, is to describe a procedure based on the operative exposure and investigation of the site of cavitation as developed in the past 2 years. The results which have been obtained can be referred to only tentatively at this time and variations in the operative steps which are at present contemplated may appreciably alter the results in future cases. It is the principle of the exposure and investigation of the lesion and the application of suitable measures in accordance with the findings which the writer wishes to stress.

Bronchography was employed routinely to investigate the situation and extent of cavities and associated fibrosis and possible bronchiectasis and the report on the result of this procedure is made as follows:

- 1 The site of cavitation
- 2 The differentiation between cavity and bronchiectasis.
- 3 The site and extent of the bronchiectasis, with its inferential evidence of fibrosis
- 4 The status of the bronchial tree in the other lobes.
- 5 The effect of operation on the cavity and adjoining bronchial tree
- 6 The reasons for failure or incomplete collapse after operation

Primarily, the technic in the early stages follows closely that of the upper thoracoplasty, with mobilization of the scapula. The approach to the lesion is obtained by subperiosteal costectomy of several upper ribs. The author states that the cavity is usually situated near the surface, only a thin shell of lung ordinarily separating its roof from the visceral pleura. The lesion can, therefore, be palpated, and seen to a varying extent, after reflexion of the musculoperiosteal flaps. It may be soft and collapsible by direct pressure or by pressure toward the mediastinum applied against the lateral stumps of the cut ribs. Collapse may be aided by extrapleural stripping around the site of the cavity. The pleural cleft was diffusely sealed by adhesions over the lesion in all cases. When there is pronounced thickening of the pleura, however, adequate collapse of the cavity does not occur with the simple manipulations that have been mentioned. No alteration in size and shape will be noted in the old stiff-walled lesions. The step which the author has termed "cavernolysis" is carried out if inadequate or no collapse occurs because of the thickened agglutinated pleuræ.

*Technic*—It consists in excising the scar-like tissue layer by layer and by piecemeal until soft less-resistant tissue is encountered. The dissection is carried out on the posterior rather than the vertebral aspect of the lesion, because collapse toward the mediastinum is desired. The excision is completed when a well-defined dimple or depression, which is characteristic of a sinking-in of wall, is felt (and often seen). The cavity has not as yet been entered in any instance, although pulmonary tissue has been cut into on a few occasions. Whether or not lysis is employed, operation is terminated by laying the musculoperiosteal

flaps in the paravertebral gutter, snugly packing iodoform gauze against the released cavity, drawing the scapula in position and layer closure of the wound about the gauze pack. The pack is used to steady the mediastinum and to induce a rigid bed at the site of the released cavity. It is usually left in place for 6 weeks, when it is withdrawn and not replaced.

The operation can usually be done in one stage for the smaller and softer cavities, but several stages through different approaches may be required for the larger, multilocular and more resistant lesions.

The only criteria by which the author estimates the *result* of operation are the disappearance of tubercle bacilli from the sputum, together with x-ray proof of collapse of the cavity. The study of the ordinary film is further amplified by bronchography in order to aid in the interpretation of any areas of rarefaction that may be noted.

*Results.*—Patients, 34, operations, 56 Collapse of cavities, negative sputum; discharged, 16 One death One case closed, with failure to collapse rigid cavities In one elderly male, a poor operative risk, the cavity was reduced to a cleft; further operation was not advisable In 9 cases, satisfactory progress toward collapse was made by 1 or 2 operations The remaining 6 were too recent to evaluate results

**PULMONARY CARCINOMA.**—Pulmonary carcinoma is no longer a subject for discussion by the pathologists alone The pathologists have demonstrated an increased incidence of the disease in the last two decades, the examinations by x-ray and bronchoscopy have brought the possibilities of positive diagnosis from the autopsy room into the clinic, and the gradual improvement in operative technic is evidenced by the increasing number of reports of successful lobectomies and complete pneumonectomies This combination of circumstances, increase in frequency, greater possibilities of early diagnosis, and demonstrated safer technic, stimulates the study of the subject from every possible angle

*Classification*—The morphologic study of 100 autopsied cases leads C. B. Rabin and H. Neuhof (J. Thoracic Surg. 5: 147 (Dec.) 1934), like others, to separate them into 2 great groups, which they term the "circumscribed" and "noncircumscribed" forms Although all are cases of cancer, there is a great contrast in the gross appearance The circumscribed type was found in one quarter and the noncircumscribed type in three-quarters of the cases observed by the writers

By a *circumscribed tumor* is meant one which has that appearance on gross examination The term is implied in contrast to a noncircumscribed or infiltrating growth A *main bronchus* cancer is one which is situated in and involves the wall of a main bronchus A *branch bronchus* cancer grows from one of the divisions of a stem bronchus By a *parenchymal cancer* is meant a growth which is situated in the substance of the lung, and is not visibly derived from a main bronchus or a macroscopic branch bronchus A peripheral cancer is situated out near the surface of the lung

**CIRCUMSCRIBED FORMS**—1 *Parenchymal cancer* comprises about half of all the cases of the circumscribed variety. As already stated the term refers to the situation and not to the source of the growth. They are so clearly delineated that tangential sections, taken a few millimeters from the neoplasm usually show no

infiltration by the tumor even when examined microscopically. Rudimentary capsule formation is often to be seen about the growth. The capsule is infiltrated by the proliferating cells. The tumor is usually not large and the lymphatic channels appear to be free from cancer cells. Even at autopsy the regional nodes may be uninvolved microscopically. Patients suffering from parenchymal tumors die of distant blood-borne metastases and not of the pulmonary neoplasm. The characteristics which have been described obviously class parenchymal tumors as a most favorable variety for surgical removal.

In a small percentage of the cases of parenchymal cancer the growth assumes large proportions and at postmortem examination occupies all or almost all of

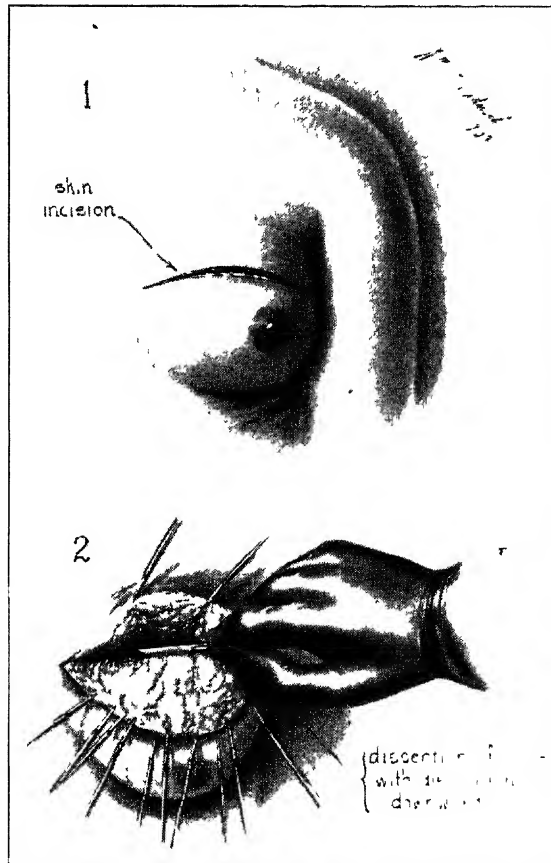


Fig 5—Operative technic (Rienhoff and Broyles J A M A)

the lobe of the lung. Rabin and Neuhoof (*loc cit.*) term this variety the lobar type. The occurrence of such large growths with little or no involvement of the lymph nodes in all the cases which have come under their observation, indicates that in these cases also there is very little tendency for the neoplasm to spread along lymphatic channels. Autopsy examination leads to the impression that these growths, too, can be placed in the class in which radical extirpation may be feasible.

2. *Peripheral Cancer (Branch Bronchus Localized Type).*—The remaining half of the circumscribed cases of cancer of the lung belongs to this group. The

tumors originate from branch bronchi of medium to small size, and the direction of their growth is outward. They are of a more infiltrative nature, but are unique because the infiltration progresses peripherally. They form a dense mass of neoplastic tissue which is sharply circumscribed on its central aspect, but which invades the lung peripherally to the pleura. In many cases the invasion extends through the pleura to involve the chest wall or diaphragm and may partially destroy overlying ribs. In spite of the peripherally diffuse or invasive characteristic, the central limits of the growth remain sharply circumscribed, so that sections taken just mesial to the neoplasm are usually free of carcinomatous invasion. Another feature of branch bronchus peripheral carcinoma is the slight

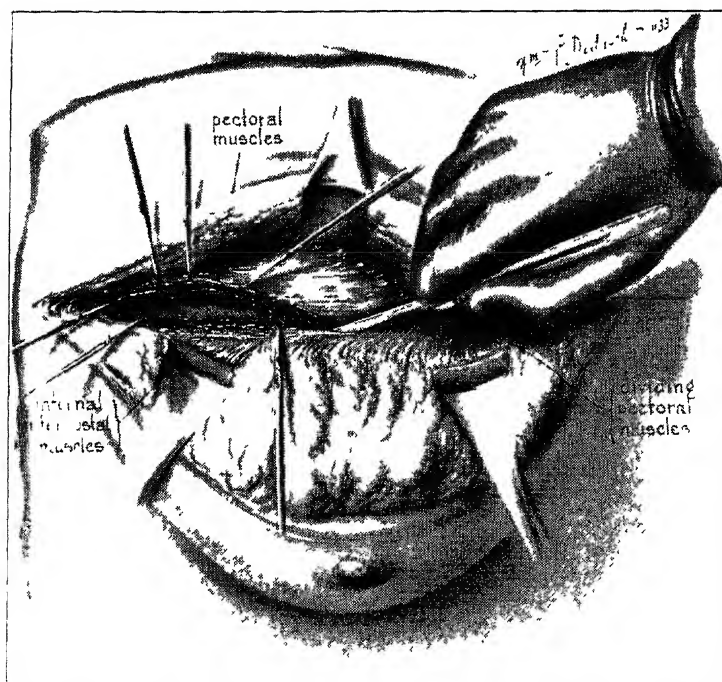


Fig. 6.—Operative technique (Rienhoff and Broyles, J. A. M. A.)

or only moderate and late invasion of regional lymph nodes. In a number of the autopsied cases, no lymphatic metastases could be demonstrated, this group, too, falls into the class in which operative treatment has favorable possibilities.

**NONCIRCUMSCRIBED FORMS**—*Main bronchus* and *branch bronchus* tumors account for all the carcinomas of the lung of the noncircumscribed or infiltrating type, and comprise three-quarters of the total number of cases. All of the neoplasms arising from the main bronchi or from the main bronchi to the lobes fall into this group. Included as well are about half the neoplasms arising from branch bronchi. Characteristic invasive features were found in almost all the cases at autopsy. As compared with the localized forms which have been described, these bronchus cancers, as a whole, show the striking contrast not only of spread, but also of extensive and (presumably) early regional lymph node involvement. It is a permeating form of cancer as compared with what might be termed the accident of spread of the localized type. From their observations the

writers conclude that the great majority of patients with main bronchus cancers are not operable by the time they become sufficiently ill to enter the hospital.

Some additional data may be summarized as follows:

- 1 Except in rare instances, the parenchymal type of neoplasm grows concentrically and by expansion and does not change into an infiltrating or noncircumscribed type.
- 2 In only two of the localized neoplasms in the series observed by Rabin and Neuhof were there lymph nodes demonstrable clinically or by the x-rays
- 3 In the noncircumscribed type of neoplasm there are clinical and/or radiographic evidences of involvement of the mediastinal or cervical lymph nodes in a large proportion of the cases by the time patients come under hospital observation.
- 4 In the instances of the noncircumscribed type in which there was no clinical or x-ray evidence of lymph node involvement during life, widespread metastases were found at necropsy

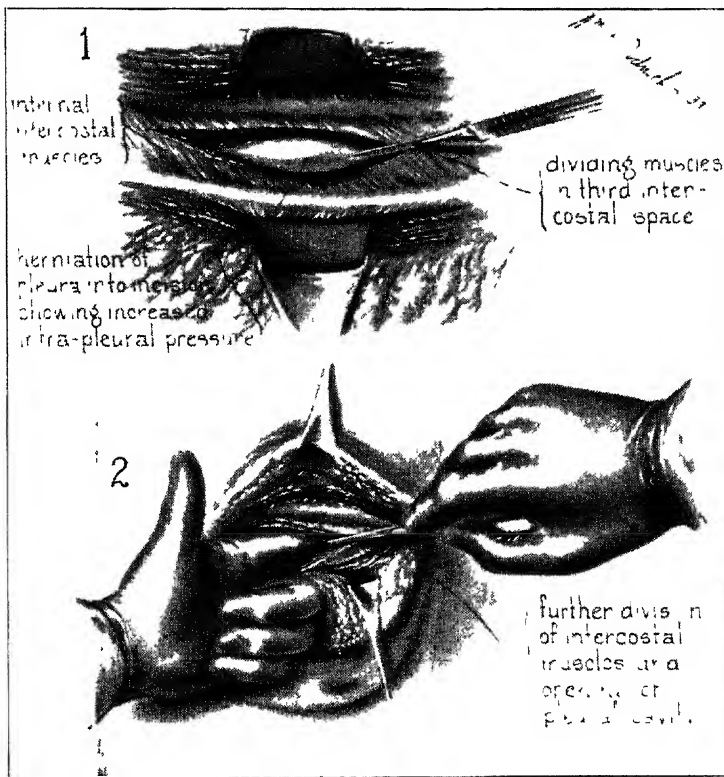


Fig 7—Operative technique (Rienhoff and Broyles I A M A)

- 5 In cases of bronchus cancer which presented a negative x-ray picture shortly before death, the regional lymph nodes were found extensively diseased at autopsy

A consideration of the foregoing leads to an alternative topographic classification which may perhaps be termed a surgical one. In such a classification, designed for operative purposes, cancers of the lung would be grouped into 2 classes—(1) Tumors of the root zone and (2) tumors of the parenchymal zone. In the first group would be placed the large bronchus neoplasms. These would generally fall into the inoperable class. In the tumors of the parenchymal zone would be placed, first, the compact tumors occupying more or less of the lobe, second, the peripheral tumors which are essentially peripherally invasive. These two groups would fall in the more favorable operative class. There would remain a small group of secondary and tertiary bronchus tumors which occupy the parenchymal zone, but are centrally invasive and therefore are in the same class as those of the lung root zone.

**Symptoms.**—In an analysis of 73 cases, A. T. Edwards (J. Thoracic Surg. 4: 107 (Dec ) 1934) records the following symptoms:

1. *Cough* was present in every case in the series except one and can, therefore, be considered an almost invariable symptom. In many cases it is non-productive, being of a dry, irritating type.

2. There was a definite amount of regular *expectoration*, which was generally of a mucoid frothy type, in 64 per cent. Occasionally the sputum is definitely purulent and may resemble that encountered in cases of bronchiectasis or pulmonary abscess.

3. *Hemoptysis* of a greater or lesser degree occurred in 87.7 per cent of patients and varied from a little staining to a brisk hemorrhage.

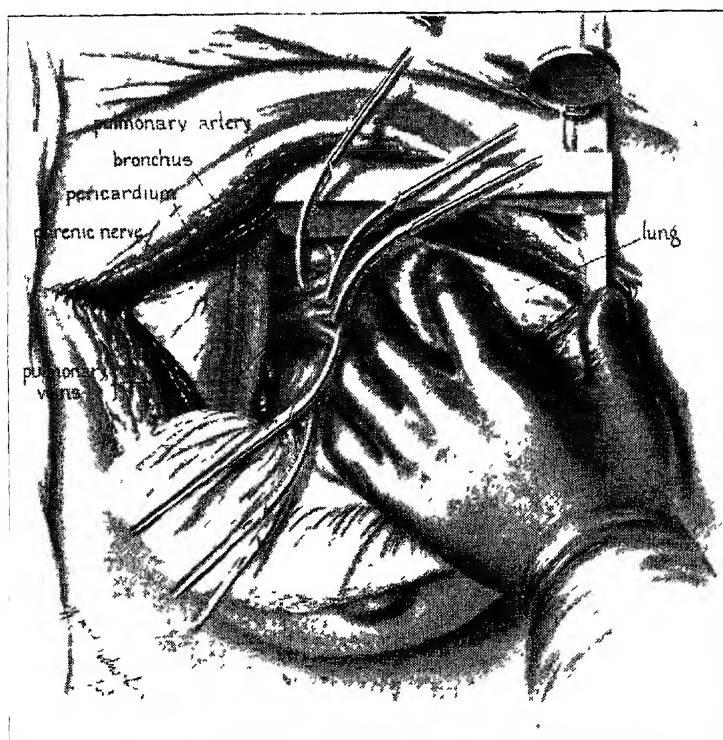


Fig. 8—Operative technique (Rienhoff and Broyles, J. A. M. A.)

4. *Dyspnea* was present in 74 per cent and does not appear to depend upon the amount of lung tissue put out of action by the disease. This may be due to involvement of branches of the vagus nerve or to toxic absorption.

5. *Pain* was variable, but was present to a greater or lesser degree in 60 per cent of the cases. It varied from an occasional feeling of discomfort to an intense neuritis, due to the growth invading the chest wall and involving the intercostal nerves.

In discussing the symptoms of pulmonary carcinoma Rabin and Neuhof (*loc. cit.*) state that *cough* and *hemoptysis* result from the ulceration of tumors of the larger bronchi, or from infection of the lung beyond an obstructing tumor to one of these bronchi. Cough is a symptom which depends largely upon the involvement of the larger bronchi, and although it is absent in the main bronchus tumors,

which are nonulcerating and nonstenosing, it constitutes one of the earliest symptoms in this group of pulmonary neoplasms. On the other hand, in the case of a peripheral or parenchymatous tumor, cough either is entirely absent, or occurs as a late symptom from pressure on the main bronchi.

The most common signal symptom of the circumscribed tumors of the smaller bronchi (peripheral carcinoma) is *pain*. It is due to the peripheral spread of the neoplasm and its gradual extension to the pleura and to extrapleural structures.

The *parenchymal neoplasms* usually cause *no local symptoms* and, because they are situated beneath the surface of the lung, rarely induce abnormal physical signs. Only when they attain considerable size, do they cause *cough* from pressure on the bronchi or give rise to *pain* from involvement of the pleura. The

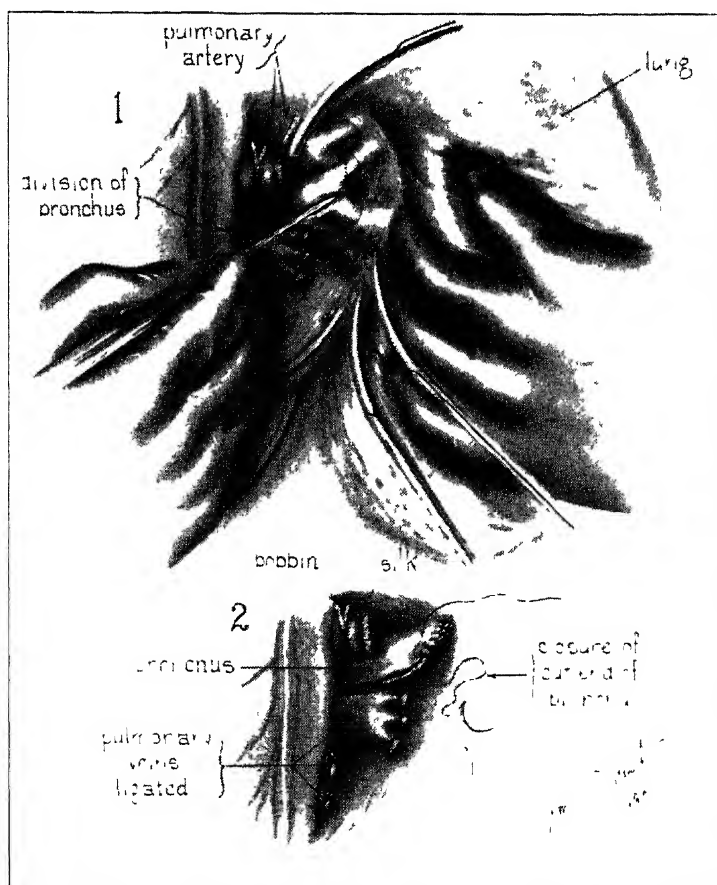


Fig 9—Operative technic (Rienhoff and Broyles J A. M. A.)

symptoms are only a general feeling of ill health and loss of weight, or the first signs may be referable to a distant, blood-borne metastasis. Clubbing of the fingers, which usually occurs early in this as well as in the other types of neoplasms, may be the only lead to the diagnosis.

**Diagnosis.**—*Clinical Signs*—The clinical signs vary considerably, depending on the situation of the growth, according to Edwards (*Ibid*). Where it occurs in the main bronchus of a lobe, the signs will generally be those of bronchial obstruction, causing atelectasis of the involved lobe. These consist of dullness



on percussion over the affected area, absence of breath sounds, and generally increased vocal resonance associated with displacement of the mediastinum to the affected side. In the lower lobes this can be determined clinically by the position of the heart's apex beat.

In those cases in which the carcinoma arises in the more peripheral parts of the lung, probably arising in secondary or tertiary bronchi, physical signs may be absent or only be those of a relatively small localized area of dullness.

*X-ray Examination*—According to Edwards (*Ibid*), this examination is essential in all patients in whom there is suspicion of carcinoma and in whom there is an unexplained hemoptysis. The x-ray examination of the chest furnishes the most reliable method for the diagnosis of the localized types of neoplasms, in

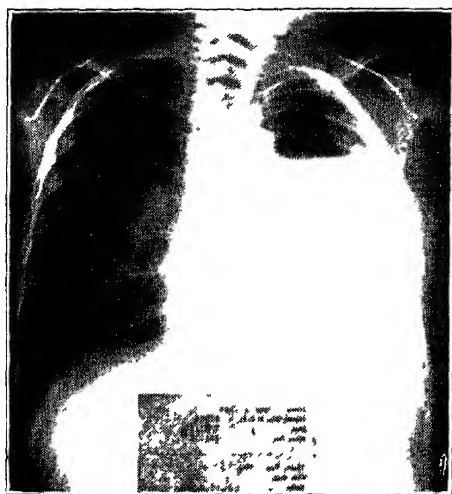


Fig. 10 (Case I, one week after operation).—Air in apex of left thoracic cavity and definite fluid level. Slight scoliosis to left side. Increased size of right thoracic cage in comparison to left. Intercostal spaces on right larger than on left. (Rienhoff and Broyles, J. A. M. A.)

the opinion of Rabin and Neuhof (*loc cit*). The parenchymal neoplasms are sharply demarcated, round shadows which may be situated anywhere within the pulmonary fields. Occasionally, they present a fluid level which may simulate the shadow of a lung abscess. The differentiation may be most difficult from the x-ray examination alone, but the absence of foul sputum, as well as the bronchoscopic and the bronchographic characteristics of lung abscess, should indicate the true nature of the lesion. In the case of the large parenchymal neoplasms which occupy an entire lobe, the picture may be confused with that of an ordinary consolidation. The convex border of the shadow of a lobar neoplasm, however, serves to differentiate it from a pneumonic consolidation.

The circumscribed tumors of the branch bronchi (peripheral tumors) cast well-demarcated shadows extending to the surface of the lung, widening as they reach the chest wall. Careful inspection may disclose more or less destruction of a rib. These neoplasms break down and discharge their contents into the bronchi more frequently than do the parenchymal growths and then simulate the x-ray appearance of a lung abscess.

The value of the x-ray examination of the carcinoma suspect is two-fold, as it is in many other instances, indicating, as it does, not only the evidences of the presence of malignancy, but also giving reliable information as to the operability of the patient under consideration.

A practical classification of pulmonary carcinomata, based on the x-ray findings, especially in its bearing on operability, is made by Rabin and Neuhoef (*loc. cit.*). A study of more than 250 cases of carcinoma of the lung, seen at the Mount Sinai Hospital in the past 10 years, has led them to conclude that such considerations are of no clinical usefulness. On the other hand, the gross examination of 100 autopsies has indicated leads of clinical value so far as operative treatment is concerned.

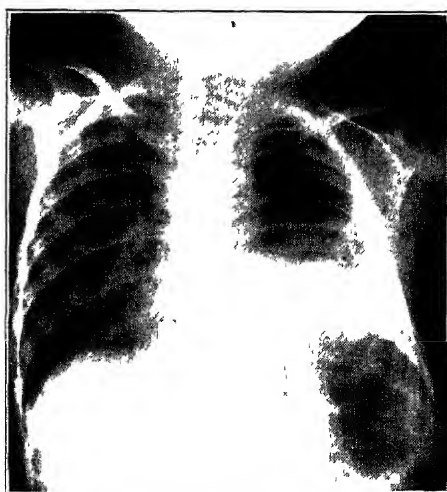


Fig 11 (Case 1, two weeks after operation) —Practically all fluid absorbed from left thoracic cavity and mediastinum being pulled over to left. Fibrous bands seen forming fenestrated labyrinthine cavity on left side. Scoliosis is somewhat more pronounced. Inter-costal spaces are relatively very much reduced in comparison to right side. Heart is in transverse position and diaphragm somewhat elevated. (Rienhoff and Broyles. J. A. M. A.)

*Bronchoscopy*—It is considered by Edwards (*loc. cit.*) that the value of this diagnostic measure in suspected malignant disease of the bronchi cannot be overestimated. When the primary growth arises in the main bronchi, or at the immediate commencement of the secondary bronchi, it is the most simple positive measure of diagnosis at the disposal of the clinician.

*Artificial Pneumothorax*—The introduction of air into the pleural space, when it is not prevented by adhesions, may serve to distinguish tumors of the inner chest wall and pleura from those arising in the pulmonary tissue and, therefore, may be of considerable value if the question of operation is being considered.

*Thoracoscopy*—This method may also add to knowledge of the conditions present within the pleura and give evidence of secondary involvement of the pleura, a condition which would contraindicate any attempt at radical operation.

*Pleural Effusions*—A positive diagnosis may be made by the Mandlebaum method of examination, which consists of the withdrawal of a quantity of fluid, subjecting it to centrifugalization, pouring off the supernatant fluid and hardening

the deposit by formalin, after which it is prepared for microscopic section and examination, as is the usual solid section. This method may be used for sputum in suspected cases.

*Exploratory Thoracotomy*.—Necessarily, this method should be employed last, and particularly in cases in which the diagnosis cannot be arrived at by other methods. By modern methods it entails no greater risk than abdominal exploration. In 2 patients with suspected malignant disease, exploratory thoracotomy disclosed teratomas, one being of enormous size, both of which were removed successfully.

*Treatment*.—With the establishment of a diagnosis of cancer of the lung, the question of therapy must needs be given immediate consideration. An un-



Fig 12 (Case 1, on discharge from the hospital).—The trachea somewhat displaced to left fibrous adhesions filling left thoracic cavity, and heart and mediastinum pushed over to left side. Diaphragm not quite as elevated as in Fig 11. At this stage, physical signs indicated that right lung had already migrated into left thoracic cage. It is to be noted here that intercostal spaces on left side more nearly approximate right side than at any time previously. Diaphragm is also in a much more normal position. These changes suggest that, as left thoracic cage fills with expanding right lung, respiratory movements may tend to normal and approximate those of normal respiratory excursion of diaphragm and thorax. (Rienhoff and Broyles. J. A. M. A.)

qualified or unamplified diagnosis of carcinoma is not sufficient, because determination of the method of treatment requires full details concerning situation, as has already been noted, and also of clinical and radiologic evidence of local (intrathoracic) lymphatic metastasis, or of distant (blood-borne) osseous, visceral or intracranial secondary growths.

Where investigation gives positive signs of metastatic lesions, palliative therapy only is justifiable. This will likely take the form of local application of some type of **irradiation** treatment with a view to decreasing the bulk of the tumor mass and retarding its lymphatic spread, in order to facilitate bronchial drainage; and, in the meantime, other general measures of relief will be used as indicated.

Edwards (*loc cit*), in presenting the results obtained by the intrabronchial use of specially devised **radon seed** containers, says "The end-results as regards cure are necessarily poor, owing to the late stage at which the diagnosis is made

There have been, however, some very definite effects. In quite a large proportion of cases it is possible to effect a disappearance of the growth in the bronchus. This has been repeatedly seen when the patient has eventually died of extension of the disease in the lung, and has a definite value of its own. Many of these patients suffer from the effects of the retention of pent-up secretions behind a growth, resulting in high temperature, wasting, and general malaise **Canalization of the bronchus** will relieve these secondary conditions, and there is often surprising improvement in every respect."

The main point at issue is the determination of the proper course in the instances where clinical, x-ray and bronchoscopic evidences are strongly suggestive of the fact that the lesion is still a localized process. Shall it be irradiation, surgery, or a combination of these measures?



Fig 13 (Case 2) —Lateral view of left thoracic cavity, 3 weeks after operation, showing different fluid levels in multilocular spaces formed by space occupying fenestrated labyrinths of connective tissue fibrous bands (Rienhoff and Broyles J A M A)

Again citing Edwards, and in sequence with the immediately preceding quotation, he continues: "Furthermore, the disappearance of the local growth is a definite indication that if these patients are seen at an early stage, there is a definite hope of curing them by **irradiation** as there is in the early carcinoma of the tongue. In fact, the patient in one of the early cases of carcinoma of the right bronchus who was first treated by this method in 1931 not only is still alive and well, but there is no evidence of growth except for the white scar in the bronchus when examined a few weeks ago; that is 3 years' freedom from recurrence. Several other patients are alive from periods of 2 to 3 months to over a year. Nevertheless, it cannot be denied that the majority of 32 patients submitted to this treatment have died of their growths."

**Radical surgery**, or combinations of **irradiation and radical surgery**, each have their advocates and the final decision may only be reached after examination by means of an open **exploratory thoracotomy** through an intercostal

incision. This has its parallel in the exploratory abdominal section, that determines the surgeon's course in carcinoma of the large bowel. Of this procedure, Edwards (*loc. cit.*), says: "First, it makes the diagnosis certain; second, it gives the patient the chance of radical operation if the growth is operable; and third, it gives an opportunity for the insertion of radon seeds if radical procedures are out of the question."

Of a group of 27 persons subjected to this **combined procedure** by Edwards, analysis shows that an average length of survival is 12 months after operation. Many of these patients have been relatively well and able to resume their occupations for some months before relapse occurs. Others have been relieved of intolerable pain, and in some patients there has been a temporary gain in weight



Fig. 14 (Case 2) —Iodized oil injection, April 25, 1934, showing filling of dilated end of descending left primary bronchus. A threadlike stream of iodized oil seen coursing down over mediastinal side of cavity connected with bronchus. Diminution in thoracic cage on left side similar to that observed in case 1. Taken with patient sitting in upright position. Silver wire sutures have begun to break up in small pieces. (Rienhoff and Broyles, J. A. M. A.)

of even as much as 42 pounds. One patient is alive and symptomless 4 years after operation; another 2 years, another 20 months."

Operative and postoperative details are important. First consideration should be given to **preliminary pneumothorax**. W. F. Rienhoff, Jr and E. N. Broyles (J. A. M. A. 103:1121 (Oct. 13) 1934) say that it serves two valuable purposes, *i. e.*, first the patients are able to adapt themselves to breathing with the noncollapsed lung and also adjust themselves to the altered conditions of intrathoracic pressure that would exist during and after the operation, thus, the shock attendant on opening the pleural cavity is negligible. The second purpose is to remove the lung mechanically as far as possible from the operative field so as to give the maximum exposure of the mediastinum with the minimum handling of the lung. Thus the operative removal can be accomplished through a relatively small incision in the chest wall; again, the necessary handling of the lung is

reduced to a minimum and the opportunity for massaging emboli from a malignant tumor is lessened.

Regarding location of the *incision*, Edwards (*loc. cit.*), in discussing 2 cases of **total pneumonectomy**, records that both the patients were operated on from a posterior incision which offers definite difficulties in the approach to the hilum if the growth is at all bulky. It appears to Edwards that in such cases an anterior approach to the hilum and control of the blood supply might be advantageous

Rienhoff and Broyles (*loc. cit.*) theoretically answer this and demonstrate the correctness of the answer in their report of 2 successful one-stage, complete, unilateral pneumonectomies. The approach to the hilus of the lung through an incision in the anterior chest wall is selected by these surgeons because, from the anatomic as well as the surgical standpoint, it is the most rational and simplest



Fig. 15 (Case 2) —April 25, 1934, after injection of iodized oil, with patient in recumbent position. Demonstrates size of cavity connected with small threadlike opening that has persisted since about 3 weeks after operation. This opening, it is believed, is diminishing constantly. (Rienhoff and Broyles, J. A. M. A.)

route. The hilus of the lung is thus completely exposed, so that an anatomic dissection may be deliberately and carefully performed. Thus, the pulmonary artery and veins may be independently and securely ligated. A second but still an important consideration is the ligation of the pulmonary veins before the lung is handled, preventing, of course, the escape of carcinomatous emboli into the peripheral circulation through the left auricle. An excellent exposure to the mediastinum may be obtained at the level of the third interspace anteriorly, which permits of a dissection of not only the lymph glands of the hilus, but also those of the posterior mediastinum as well.

This incision is laid, as noted, in the third interspace, from the parasternal to the anterior axillary line, and by rib retraction, without fracture, gives the required exposure.

The *bronchial stump* was cared for by cutting the cartilaginous bronchial rings at several points, suturing of the mucosa with number 1 plain gut and approximation of the wall with interrupted silk. The vessels having previously been closed individually with silk, there was no massive stump nor cauterized bronchus to provide slough.

The question of *drainage* in this type of operation and lung root treatment is answered by complete, tight closure in each instance

Rienhoff and Broyles consider that thoracoplasty is certainly unnecessary in pneumonectomy. A sterile small pneumothorax is harmless, yet even that condition will be rare, for the cavity remaining in the thorax after the maximum compensatory dilatation of the remaining lung will gradually obliterate itself by the formation of multiple fibrous bands, creating a veritable fenestrated labyrinth of many small spaces.

The following summary is made by these writers, as covering the important points of the method of operation

- 1 The preliminary collapse of the affected lung
- 2 The anterolateral incision and approach
- 3 The isolation and separate ligation of the pulmonary vessels
- 4 The primary closing of the bronchus after the cartilaginous spring has been interrupted
- 5 The primary closing of the chest wall without drainage
- 6 The prevention of postoperative sloughing and formation of bronchial fistulas
- 7 The avoidance of resection of ribs and especially of thoracoplasty with its consequences
- 8 The prevention of shock
- 9 The comparatively short duration of operation, and early convalescence

**THORACIC INJURIES.**—The occasional peculiar masking of the great severity of some thoracic injuries and the imminence of profound shock by an early slow pulse, is noted and attributed by C. A. Hedblom (Surg. Gynec. and Obst. 58: 503 (Feb. 21) 1934) to an injury irritation of the vagus and, possibly, of the thoracic sympathetic nerves. An initial slow, full pulse due to such vagus stimulation may lead to an underestimation of the seriousness of the injury. In one such instance observed by the author, the patient was able to give a clear account of the automobile accident in which he was injured. A few hours later he was dead from shock.

The search for the presence of positive *pneumothorax* is indicated, and the institution of treatment advised. A tension pneumothorax, proved by manometric readings, or by the rush of air out of the aspirating needle, may be relieved temporarily by simply **allowing the air to escape** or by **aspirating** it, but if increasing dyspnea develops repeatedly, an open **thoracotomy** is indicated for closure of the valve opening.

A *hemothorax* that does not produce symptoms of blood loss or dyspnea from crowding the mediastinum to the opposite side, should be left undisturbed for several days at least. Aspirating blood at once will produce reexpansion of the lung in proportion to the amount of blood withdrawn, and this may lead to recurrence of hemorrhage, which may be serious if superimposed on previous blood loss. A recurrent leakage of air from a communicating bronchus may also

result. Dyspnea and cardiac displacement may, however, necessitate **aspiration** of a portion of the hemothorax to relieve the mechanical embarrassment to the other lung. Increasing pallor, a steadily climbing fast pulse, and physical evidence of an increasing hemothorax, call for **transfusion** first, then **thoracotomy** for controlling hemorrhage, and, in case of severe laceration of the lung, for **repair** of that condition. Hemorrhage is the most frequent cause of death during the first 24 hours after thoracic injury.

Hedblom states that it is important to recognize that an infection may be present in aspirated blood that shows no physical change.

A *traumatic empyema* is of more serious import than the ordinary post-pneumonic type from the standpoint of both prognosis and treatment. Complicating a pneumothorax with complete collapse of the lung, the infection involves the whole pleural cavity, and the resulting toxic absorption is correspondingly great. Such empyemata are also prone to become chronic, due to the early tendency for the lung to become fixed in the collapsed position.

The **closed method of drainage with hypochlorite solution** is especially suitable for empyema complicating pneumothorax pulmonary collapse. The extensive suppurating pleural surface can be washed clean, the hypochlorite exerts a bactericidal effect, and the aspiration of fluid until less than atmospheric intrapleural pressure is produced assists in the reexpansion of the lung. If the lung injury is present, the closed method with salt solution or nonirritating antiseptic solution irrigation should be used in the early stages of treatment. If there is *persistent bronchial fistula*, **open drainage, with silver nitrate stick** to the bronchial stoma, will usually prove sufficient for closure. **Dakin solution irrigation** may be used.

**TRAUMATIC ABSCESS.**—Abscess symptoms usually begin in from 1 to 5 weeks, according to Hedblom (*Ibid*), but may follow years later. He reports removal of a piece of wood, through a **thoracotomy** incision, 10 years after an injury, the patient being symptom-free until 3 months before operation.





# Urology

*by*

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**BLADDER.—CORD BLADDER.**—Due to the more careful study of cases of bladder dysfunction and the more complete coöperation between the neurologists and the urologists, a series of cases is being seen today which requires careful diagnostic judgment and more careful, thorough treatment planning.

H W Walther (*Urol and Cutan. Rev.* 38: 651 (Sept.) 1934) in an excellent article states that there are 2 groups, broadly, of cord bladder: (1) syphilitic myelitis; and (2) the spinal injury patient. The diagnosis in either case is not particularly difficult. They are both, as a rule, cases of overflow retention. In the event of the history of injury to the spinal cord, a diagnosis of bladder paralysis is easily made and seldom requires cystoscopic examination. The cases of syphilitic myelitis are more complicated. Many of these patients are sent into the hospital with the overflow of retention diagnosed as bladder neck obstructions of one type or another. The cystoscopic picture in these cases is almost diagnostic, and the neurological examination plus the serology of both the blood and spinal fluids confirms the diagnosis.

In a study of 250 cases of cord bladder by F. C. Lendrum and F. P. Moersch (*J. A. M. A.* 102: 658 (Mar. 3) 1934), the conclusion is that this is a disease practically affecting males. About one-half of the patients came to the hospital for the treatment of urinary symptoms and the balance because of neurological symptoms. The condition is not incompatible with long life. The chief cause is syphilis of the central nervous system and myelodysplasia, or developmental defect of the spinal cord. All vesical function disturbances should be given both careful neurological and urological surveys.

M B Wesson (*Urol. and Cutan. Rev.* 38: 572 (Aug.) 1934), in a powerful plea while discussing the traumatic cord bladder, insists against the use of the catheter to relieve the overdistended, nonobstructed cord bladder. He believes that with a little **morphine** and patience most of these cases may be converted into automatic bladders within 96 hours, and pleads not to convert a good neurosurgical case into a urological one by the routine use of a catheter because of the great danger of sepsis. He states that in the majority of these cases death is not due to traumatic transverse myelitis, but to general sepsis. Much work has been done in attempting to treat these cases and return them to as near a normal condition as possible. Wesson states that in order for a bladder to evacuate its contents normally and at appointed times, all the paths to and from the central nervous system must be intact, and yet there is no doubt that the fully decentralized bladder is capable of automatic, if feeble, contraction and discharge of urine. Following cord injury there is a lax condition of the bladder musculature as a whole, accompanied by a considerable amount of spasm at the neck of the bladder.

E D McCrea and A. D. MacDonald (*Brit. J. Urol.* 6: 119 (June) 1934), in a very careful experimental study on the nerves that control micturition, confirm a fact which is considered correct, that the sympathetic and parasympathetic nerves function together in the regulation of the bladder and that the parasympathetics are by far the more important. While the action of one or other may be

predominately excitor or inhibitor, yet it is not to be assumed that either is exclusively so, nor yet that they are antagonists. It is known that both nerves transmit sensory impulses, the pathway by the pelvic nerves being the more important. The precise action of the hypogastric nerves on the vesical sphincters is not known; nor, indeed, is it known that they have any influence at all upon them.

J R Learmonth (Proc Staff Mayo Clin 6:182, 1931; Jour Urol 26:13 (July) 1931), a few years ago, studied a series of cord bladder cases and treated them by **presacral sympathectomy**. His work was revolutionary in the treatment of this type of bladder dysfunction. In the luetic cases treatment could be considered under the following heads:

- 1 Administration of **antiluetic medication** and internal urinary **antiseptics**.
- 2 Establishing automatic emptying of the bladder by **reeducating the muscles and nerves of micturition**.
- 3 **Dilatations** of bladder neck with bougies, sounds or Kollman dilators, **prostatic massage**.
- 4 **Sinusoidal or morse wave galvanic current** through the bladder area
- 5 Intermittent or indwelling **catheter drainage**.
- 6 Caudal or spinal injections of **procaine**.
- 7 **Punch operation** or **electric loop resection of vesical neck**.
8. Exposure of bladder neck and **removing V-shaped section from posterior urethral lip**.
- 9 **Suprapubic cystotomy drainage**.
- 10 **Section or resection of presacral nerve plexus**.

The reviewer has had several very interesting experiences in the treatment of cord bladders by **presacral ganglionectomy**. The operation was done on 2 patients who had overflow incontinence of urine of 6 years' duration with residuals of urine of 60 ounces and 30 ounces respectively, complicated by severe genitourinary sepsis from catheterization. At the present time they each have less than 5 ounces of residual urine and have 8-hour control with no dribbling. Presacral ganglionectomy is indicated in all cases of vesical paralysis in which the lesion is situated in the parasympathetic pathway and where the parasympathetic is intact. This operative procedure, of course, should not be used unless the patients fail to respond to other forms of treatment. Learmonth warns against its general adoption in the treatment of neurogenic dysfunction of the bladder.

**DIVERTICULOSIS.—Diagnosis.**—The diagnosis of diverticuli of the bladder is made by the cystogram and cystoscopic examination. Occasionally it may be suspected from the patient's subjective urinary history. Given a patient who voids and believes he has emptied his bladder and then a few minutes later is required to void again and voids a large, or fairly large quantity of urine, the diagnosis may be suspected. Usually, however, the subjective symptomatology is overlooked by the patient unless some complicating condition causes urinary symptoms to become more acute. Briefly, the two pathological entities

that will exaggerate the urological disturbance are infections, including stone, and newgrowths.

A. A. Kutzmann (Urol. and Cutan. Rev. 38:634 (Sept.) 1934) and R. H. Herbst (J. A. M. A. 102:188 (Jan. 20) 1934) discuss the diagnosis and treatment in the two sexes. Kutzmann believes that diverticula of the female urinary bladder is of infrequent occurrence; that it is usually easily recognized by the cystoscope and urography. In the female it is usually a disease of old age. *Treatment* in all cases is directed toward the etiological condition. Surgery is not indicated. In the male, however, this does not hold true. According to Herbst, all retention diverticula are found in the male and must be removed if it is hoped to obtain a good result. The early correction of the milder forms of bladder neck obstruction, such as fibrosis and median bar, may prevent formation of diverticula of the bladder and serious renal damage.

**TUMORS OF BLADDER.**—The *diagnosis* of bladder tumors may be made in two ways. Pfahler, of Philadelphia, without cystoscopy and in suspected cases, fills the bladder with air and takes a series of roentgenograms from different angles. He then interprets the abnormalities in the bladder wall and attempts to estimate the depth of the infiltration of the newgrowth. In the hands of a man like Pfahler a diagnosis of this character may be sufficient, but it is the consensus of opinion of men who strictly limit themselves to the practice of urology that given a certain symptom complex, examination with the cystoscope is the only sure method of making a correct diagnosis. Every patient who has painless hematuria, no matter what the age incidence, should be submitted to immediate cystoscopy. The classification of the tumor, whether benign or malignant, may be fairly correctly estimated by simple cystoscopic observation. The magnitude of the hemorrhage, as a rule, does not aid much in this deduction. Without sections it is impossible to classify any bladder tumor for scientific purposes.

Occupation may give the first indication of the presence of a bladder tumor. The subject of *anilin tumors* of the bladder is thoroughly discussed in a symposium by R. S. Ferguson, G. H. Gehrmann, D. M. Gay, L. W. Anderson and V. D. Washburn (J. Urol. 31:121 (Feb.) 1934). The majority of bladder tumors are of epithelial origin. Rehn, in 1895, discovered the anilin tumor of the bladder. The tumor is caused by a toxic agent that is inhaled or absorbed through the respiratory tract in anilin dye workers. Prior to the war, most of the anilin dyes were imported from Germany and Switzerland and by far the greater number of these peculiar tumors were found in those countries. Since the war, the manufacture of coal-tar dyes in America has assumed important proportions and any man working in this industry should be frequently examined by cystoscopic methods for the early recognition of such a tumor.

The *treatment* of bladder tumors, whether benign or malignant, has been very thoroughly developed in this country. The reviewer, E. Hess (Urol. and Cutan. Rev. 38:579 (Aug.) 1934) believes that, wherever possible, all tumors of the urinary bladder should be treated by **bipolar coagulation** through the cystoscope, followed by the implantation of **radium** and in certain selected cases by deep **x-ray therapy**. Open operation is only advised because of the

size or inaccessibility of the tumor to cystoscopic manipulation. In *inoperable and incurable carcinomas* of the bladder an attempt may be made to do a **total cystectomy** and **bilateral implantation of the ureters into the bowel**. In the reviewer's experience this has not been a thoroughly satisfactory procedure.

B S Barringer (Surg. Gynec. Obst. 58:867 (May) 1934) believes that the proper method of treatment for the large bladder tumor is **open cystostomy** with the implantation of **radium**, and that the choice of procedure as to open operation and cystoscopic treatments lies with the skillful operator.

E L Keyes (*Ibid* 58:233 (Feb 1) 1934) makes the statement that no attempt has been made to compare **cystoscopic fulguration** or **radon implantation** with **suprapubic radon implantations**. During this period more than one-half of the reviewer's bladder tumor patients have been submitted to suprapubic implantations of radon. Thanks to the practice of suturing the bladder without drainage, the postoperative mortality and discomfort are slight. Thirty-seven radon implantations are herewith reported with but one postoperative death. The second postoperative death followed resection of the bladder. The atrocious postoperative spasms that follow the implantation of glass seeds do not occur. Twenty-seven of the operations were followed by no more discomfort than is to be expected after any cystotomy. The 6 patients who required more than one operation submitted to the second without comment. Comparison between resection of the bladder and radon implantation cannot be attempted on the basis of the cases herewith reported. Cure of a localized tumor is possible by either method. Resection is not applicable to tumors about the trigone or bladder neck, though these present no peculiar difficulties to the implantation of radon. Ureteral re-implantation does not have to be considered. It is hoped that the durability of radium cure is no longer questioned. For the treatment of minor degrees of malignancy the choice of cystoscopy or suprapubic section for the implantation of radium is of no great importance, but whether applied through the cystoscope or the suprapubic wound, radium destroys malignant tumors that fulguration does not control.

All bladder tumor cases as a part of the diagnostic procedure should be submitted to x-ray examinations of the various bones of the body, because R C Graves and R E Miltzer (J Urol 31 769 (May) 1934) believe that *metastases* from a carcinoma of the bladder to bones are more common than generally supposed. A thorough search for metastases must therefore be made. They report a case of carcinoma of the bladder with metastases to the lungs, liver, and right fourth rib, histologically proven, and 4 cases of carcinoma of the bladder with x-ray evidence of bone metastases. These metastases are of the osteoclastic type, but some show osteoplastic changes. Great caution must be observed in condemning a case as inoperable because of associated bone lesions.

To recapitulate, the public and the profession must be educated to demand cystoscopic examination following any bleeding from the urinary tract. The diagnosis is positively made by cystoscopic examination. The prognosis is estimated by the experience of the operator according to the position and appearance of the tumor present, and from the biological section with Broder's Grading as set up by the Carcinoma Registration for bladder tumors of the American

Urological Association. The treatment is divided into **cystoscopic, fulguration, and radium implantations, and operative suprapubic cystostomy with fulguration and radium**, in some cases supplemented by deep x-ray therapy, and in a few cases by **total cystectomy with ureteral transplantation**.

**GONORRHEA.—Treatment.**—So much has been written about gonorrhea and its complications that there is really little left to be said about this common infection. The disease is as old as civilization and certainly is curable, yet there is no disease that has as many different forms of treatment as does gonorrhea.

The gonococcus is not a very viable organism. It is easily destroyed by changes in temperature and under aerobic conditions. It is very difficult to destroy in the particular parts of the human body where it causes the most trouble. It grows best upon the mucous membranes of the body where anærobic conditions prevail, at body temperature, and on cylindrical epithelium.

Given a urethritis caused by this organism, what then is the best method of management? The disease must be, for treatment purposes, classified into several groups: (1) As to sex; (2) acute, subacute, and chronic; and (3) anatomically

*In the Male*—*Prophylaxis* is always essential. After exposure the external genitalia should be thoroughly **cleansed with soap and warm water** and a careful injection made into the anterior urethra of **protargol** or some similar antiseptic. This should be a nontraumatic injection and the solution should be held gently in the urethra for 5 minutes. The efficiency of this prevention of the disease is in inverse ratio to the time after exposure that the treatment is given. This was very definitely proven by experience in the army. Those men who received prophylactic treatment within an hour after exposure were seldom infected. To this treatment in the army was also added **mercurial ointment** for the prevention of syphilis.

There are many men who believe in the abortive treatment of an acute anterior urethritis. There are many acute urethral discharges following exposure which are diagnosed by the attending physician as gonorrhea. Many of these will clear up in several days without any marked local discomfort and are in all probability nonspecific in origin. Organisms such as the *Micrococcus catarrhalis* are very often mistaken for the gonococcus.

In *acute specific anterior urethritis* a common practice is to give the patient a syringe and instruct him how to make an injection with some antiseptic so many times a day, usually after urination. This method of treatment is bad, because there are practically no laymen who understand anything about the disease and less about the proper method of making an injection. At this period of the disease, local treatment, except by the physician, is to be condemned, and often the patient will do better if no local treatment at all is used in the acute stage.

Various antiseptic drugs have been employed as injections and if used by the physician, care must be taken that an already acutely inflamed mucosa is in no way traumatized. A bit too much force, a bit too much injection or bruising of the tissues by various devices to hold the solution in the urethra will all



produce dangerous complications. Far better, if possible, is it to put the patient at more or less **rest**, flood him with **fluids**, give him a mild so-called **urinary antiseptic by mouth**, put him on a **liquid** or **semi-soft diet**, and leave him alone until the acute symptoms subside. The practice of putting a plug of cotton under the foreskin to catch the discharge and spare the clothes is bad, as it only locks the secretion, which should drain out, within the urethra. If the danger of injection, self-medication, overindulgence in food and alcohol are properly impressed upon the patient, with an explanation of the possible complications that are more than likely to ensue from improper management, there will be little difficulty, in the average case, in gaining the confidence and cooperation of the afflicted individual.

The average case of specific anterior urethritis sooner or later involves the posterior urethra and the adjacent genital organs. When an *acute posterior urethritis* arises, all methods of local treatment must be discontinued immediately (if they have been used) and drugs should be given to lessen spasm and to render the patient as comfortable as possible during the act of micturition.

Acute involvement of the posterior urethra is usually ushered in with an inordinate frequency, urgency, and burning on micturition. If the patient is put at rest and no local treatment is instituted, the acute condition will subside in a few days, very often it will readily and rapidly clear up with **rest**, **forced fluids**, and **mild urinary antiseptics**. During the subacute stage, instrumentation of any kind or injections of any kind are positively contraindicated unless abscess formation somewhere in the tract has taken place. After the subacute inflammation further subsides and a more or less slight chronic discharge persists, **prostatic** and **vesical massage** with lavage of the urethra and bladder with warm mildly **antiseptic solutions** may be and often is indicated.

A persistent discharge in the male should be investigated by general lower urinary tract examination and endoscopic observation and treatment may become indicated. Here, again, very often, treatment may be too intensive and a chemical or traumatic urethritis may be added to the specific infection. It should not be forgotten that any drug that can kill an organism in the human body is strong enough usually to destroy the superficial layers of the epithelium. Not only does the gonococcus invade the superficial layers of the epithelium, but the organisms work down between the cells and may be found in the deeper parts of the mucosa, well isolated from the surface. It should not be forgotten that in the vast majority of cases, gonorrhea is a self-limiting disease, and that eventually the defense mechanism of the body can overcome the infection. Naturally, the defense organisms are the polymorphonuclear leukocytes, and anything that will stimulate phagocytosis will help the patient conquer the disease. In all inflammatory conditions free drainage is the essential thing. This can usually be best obtained by **forcing** the consumption of **fluids**. If there is a small urinary meatus, it is essential that a **meatotomy** be done immediately. A complicating phimosis or paraphimosis should be relieved immediately.

In *chronic prostatitis* following acute specific posterior urethritis, it is essential to know that the prostate is very often secondarily invaded by other organisms which may be eliminated through the urinary tract, the prostate now

becomes, due to the specific invasion, a breeding ground, as it were, for other bacteria. In cases of this type, it is often very difficult to find any bacteria which resemble the gonococcus, but cultures made from prostatic and vesicular secretion may show colon bacilli, streptococci or staphylococci. It is therefore necessary, before this type of prostatitis can be thoroughly eradicated, to search for, find, and eradicate possible primary foci of infection elsewhere in the body.

In the event that an *acute epididymitis* complicates an acute posterior urethritis, the individual must be immediately placed at **rest in bed**. The **testicle** must be **elevated**, the **diet** should be **liquid or semi-soft**, and **ice-caps** or **diathermic measures** may be applied with relief of the symptoms and a subsidence of the inflammation. If an **abscess** forms in the epididymis, it should be immediately **opened and drained**.

Many drugs are used as injections and many combinations of drugs are employed in the various stages of the disease. Most of them are not only worthless, but actually harmful unless used with the greatest gentleness and caution. **Protargol**, 10 per cent., **argyrol**, 20 per cent.; **silvol**, 5 per cent.; **silver nitrate**, 0.5 and 1 per cent.; **mercurochrome**, 1 per cent.; 1-5000 **perman-ganate**; **acriflavine**, and others, all have their advocates. To say these drugs are not useful at times and in competent hands is absurd; equally absurd is it to say that their use in unskilled hands is not extremely dangerous.

The drugs that are used by mouth are many and varied. Most of them are useless and are given principally for their psychological effect. Some urologists speak very highly of **pyridium**, **serenium**, **caprocol**, **hexamine**, and many others. The most valuable drugs to use in the disease in its various stages are those which alleviate pain, strangury, and burning micturition. An acid urine will naturally irritate an inflamed mucosa; likewise, if it be highly alkaline, it may do the same thing. The urine should be carefully watched and drugs given to control the reaction. **Opium** and **belladonna** to ease pain and relieve spasm are extremely useful.

The vast majority of post-gonococcic complications, such as strictures, chronic prostatitis and vesiculitis, bladder-neck scleroses, and often epididymitis, are due not so much to the disease itself, as to the methods of treatment employed to control the acute manifestations. No treatment at all is far better than too energetic and too active local treatment. The less one attempts to treat acute gonorrhea in the male, regardless of its anatomical location, the better will be the end-results. These patients need to be impressed with the serious results of the disease if not properly handled, they need confidence and explanations as to what they have, what they may expect, and what may be the end-result of the treatment outlined for them, and upon their cooperation and intelligent management by the physician depends the ultimate result.

The idea that every person to be a man must have at least one attack of gonorrhea is a foolish conception, yet most men treat such an attack with levity and more or less braggadocio. No patient should be given a physician's permission to marry until at least two years have elapsed since his original infection and then only after repeated examinations have failed to reveal the presence of residual infection.

*In the Female.*—Here there are 2 distinct types of gonorrhea and they are managed rather differently. In female *children*, before the age of puberty, the gonococcus attacks the vaginal mucosa by preference. It may, but seldom does, cause endocervicitis, endometritis, salpingitis and peritonitis, although it may cause all of these conditions. Usually, the disease resists all forms of specific treatment until just before puberty, when for some unknown and unaccountable reason it subsides. Perhaps virgins who marry later may pass gonorrhea on to their partners, innocent of the fact that they have the disease themselves as a result of this early infection. Most observers feel, however, that the disease appears to be eventually self-limited.

Most of the trouble from the infection in these young females is due, no doubt, to too energetic treatment. All sorts and types of treatment have been advised from time to time. Perhaps one of the best ways to manage these cases is to insist on gentle genital cleanliness with a **mild soap and warm water**, followed by the insertion of 1 or 2 per cent **mercurochrome suppositories** into the vagina.

These children are particularly unfortunate, as the disease is extremely contagious, they should not be admitted to hospital wards or other places where healthy children are congregated. If there are other female children in the same household, they will all eventually get the disease unless the utmost precautions are taken to protect them. It is a real hardship for a parent to care for these unfortunates, and in institutions of various kinds it is more than a hardship for the management.

In *adult women*, acute gonorrhea attacks principally the urethra, Bartholin's glands, and the glands and mucous membrane of the cervix and endometrium, from whence it may extend to the tubes and peritoneum. Again, in women, the disease, even in the acute stage, may cause very little personal discomfort, although the usual symptoms are those of vulvar and cervical inflammation, with profuse scalding mucopurulent discharge.

As in any case of acute inflammation, treatment must be based entirely upon drainage and nontraumatic handling of the diseased parts. Solutions should be mild and nonirritating. The urine must be kept as bland and nonirritating as possible. Cleansing of the parts after voiding or defecation must be gentle. Here, douching, if used by the patient, should be done gently with bland solutions, but preferably, no local home treatment should be used in the acute stage. The irrigation of the genitalia is the physician's job or should be done by a competent nurse under the physician's supervision.

**Rest in bed, free bowel movements, forced fluids** are just as essential to the female as to the male. Drugs to keep down excessive acidity or alkalinity of the urine are indicated, and antispasmodics will often prove comforting to the patient. The external genitalia should be bathed freely but gently with soap and warm water after the emptying of the bladder or a bowel evacuation. Paper should never be used. Cotton or a soft cloth is much less irritating. Enemas should not be given because of the danger of rectal involvement during the acute stage. The patient should present herself to her physician every day, if possible. She should first be gently **irrigated with a warm, mild solution**; the **pelvis**

should then be **elevated** and the **vagina** gently filled with a **mild antiseptic solution**, which is allowed to remain *in situ* for 15 or 20 minutes. Then this solution should be gently aspirated or the table lowered so that the solution will flow out of the vagina; 5 minutes later the procedure should be repeated.

The acute symptoms, as a rule, will subside in a week or two and other forms of treatment will be necessary to clear up the residual infection. If *acute salpingitis* or *peritonitis* supervenes, **rest in bed, liquid diet** and **packing the pelvis in ice** will usually suffice to carry the patient over the attack. Often a *Bartholin's abscess* must be **evacuated**. Better to remove it completely, if possible. *Urethritis* must be treated if it develops and becomes chronic. Many women suffer from urethral strictures secondary to gonorrheal infection as do men. This condition is frequently overlooked and often requires treatment.

In *pelvic inflammation*, during the acute stage or the acute exacerbation of the chronic stage, the expectant treatment is always indicated. In the chronic stage with disabling symptoms, **laparotomy** must be done. It is often surprising how many of these women with pelvic inflammations can live comfortable lives without surgical interference if they and their physicians will take the time and trouble necessary to the gentle, careful management of their cases. **Hot vaginal douches** are often beneficial even if they are not curative. **Cauterization of the cervix with destruction of the infected endocervical glands** will often cure a *chronic gonorrheal endocervicitis*. If a woman is in the child-bearing age, conservatism should be the key note of the management of the case. E. Hess (*The Urolog* 1: 5 (Sept.) 1934)

During the last few years, gonorrhea and its complications have been treated by **gonococcus filtrate**. B. C. Corbus and V. J. O'Connor (*J. Urol.* 24: 333 (Sept.) 1930) treated 195 patients in the various stages of gonorrheal infection with their filtrate. There were 86 acute cases, 23 subacute, and 42 chronic cases in the male. In the female, there were 10 acute, 6 subacute, 29 chronic cases, and 3 girl babies. The shortest period of treatment which was followed by a complete disappearance of the gonococcus from the secretions in acute and subacute conditions in the male was 4 weeks and 9 weeks in the female. In chronic infections in the male, the shortest period of time was 1 week, and 9 weeks in the female. All of the gonococcic infections, such as gonorrheal arthritis, salpingitis, and infections of Skene's and Bartholin's glands were treated. It does seem with the observations of R. E. Cumming and R. A. Burbans (*J. A. M. A.* 104: 181 (Jan. 19) 1935) that this is the most advanced step in the treatment of gonorrhea that has been made for years.

Adults, whether men or women, having acute gonorrhea should be given initially, by intradermal injection, not more than 0.05 to 0.1 cc. of the filtrate. Overdosage should be and can be avoided by observing the cutaneous reaction at the site of injection and noting the presence or absence of signs and symptoms indicative of constitutional intolerance. Since the latter type of untoward phenomena is rare, the extent of the skin reaction, as measured by areola formation, signalizes the reactivity of the patient. Along with this peripheral manifestation occur focal reactions at the site of gonococcus infection. If the dose has been too large, adnexitis of various types and engorgement of the urogenital tract will

occur; likewise, all symptoms such as swelling, pain, discharge and any other of the numerous manifestations may be augmented.

Adults, whether men or women, having subacute or chronic gonorrhea or a gonococcus infection of a joint or the adnexa will usually tolerate initially 0.05 to 0.1 c.c. more of the filtrate than will acute cases; likewise, the size of subsequent doses can usually be increased more rapidly. The same criteria as recorded above for increasing the dose of the filtrate at regular weekly intervals must be observed. Where there is doubt as to the duration or stage of infection, the initial dose suggested for acute cases should be followed.

Using an initial dose of the filtrate as given above, the areola at the site of injection should not exceed 2 inches in diameter. Within this limit of areola formation the next dose is to be increased by 0.05 to 0.1 c.c. and given after a 6 to 7 days' interval—*never more frequently*. The same criteria for increasing the dose of the filtrate at regular intervals of one week thereafter must be observed. Under no circumstances should the dose of filtrate be increased on the occasion of the next injection when the signs and symptoms of overdosage described above have occurred. In the event of overstimulation, manifested as described, the next dose, given after a lapse of the stipulated interval, should be the same or 0.05 c.c. less than that causing the untoward reaction.

It is seldom necessary that the maximum dose of the filtrate exceed 0.5 c.c.

It is recommended that the filtrate be diluted with 3 parts of sterile normal saline for the treatment of children. An initial dose of the diluted filtrate not to exceed 0.025 to 0.05 c.c. should be given, depending on the age of the child and the stage of the infection. The dose of the diluted filtrate should be increased at weekly intervals by not more than 0.025 to 0.05 c.c., depending on the local skin reaction and the character of the discharge. The identical criteria described above should govern the selection of the dosage schedule following the initial administration of the filtrate.

Gonococcus filtrate is intended specifically for the treatment of gonorrhea and its complications. It should be used only in those cases in which the presence of the gonococcus can be demonstrated by differential Gram stain of secretions or by positive gonococcus complement fixation test. It is essential that gonococcus filtrate be given only by the intradermal route and that a definitely spaced interval of 6 to 7 days elapse between successive injections. Manifestations of hypersensitivity must not be overlooked, since they govern the dosage range.

Questions arise naturally in a consideration of therapy of gonorrhea with the filtrate described above. Does the filtrate shorten the duration of treatment of the acute infection? Are local measures necessary? Usually, consistent treatment with the filtrate in accordance with the foregoing instructions should lead to satisfactory therapeutic results in acute and subacute gonococcus infections within a period of 5 to 7 weeks. Amelioration of symptoms may occur as early as the second or third week, if the dosage has been properly adjusted to the individual, but eradication of the specific organism will usually require an additional period of treatment.

The value of mild local treatment in alleviating symptoms and disposing of irritating secretions should not be overlooked. Urethral injections in males can

advantageously be utilized in the beginning, but with the disappearance of the gonococcus from the secretions, local treatment should be discontinued, in order to avoid chemical irritation of tissue and its consequences.

*Prostatitis* usually accompanies posterior urethral involvement. Systematic **prostatic massage**, not more often than once in 5 days, as an adjunct to filtrate treatment, is recommended. Treatment with the filtrate and massage should be continued until the prostatic secretions are free of gonococci.

**KIDNEY.—ANESTHESIA.**—In operations upon the kidney the subject of anesthesia has held the attention of urologists for a great many years. **Ether**, considered perhaps the safest of all forms of anesthesia insofar as a great many surgical conditions are concerned, has been tried and more or less found wanting because of its well-known damage to the renal parenchyma. There is no question that a general inhalation anesthetic has its advantages and its disadvantages. **Gas oxygen** with some local infiltration is being used successfully at times. Because of these various disadvantages, **spinal anesthesia** has been used with success, although it is by no manner of means universally accepted by urologists.

G. S. Foulds and H. S. Douglas (J. Urol 31 607 (May) 1934) say that old prejudices, which it is believed will be dispelled by greater familiarity with the method, will still be retained by many. They have reviewed 500 case histories of patients upon whom **spinal anesthesia** was administered in order to submit a brief account of their experiences with this method of anesthesia. The requirements for a satisfactory anesthetic in urologic practice include, in addition to the factors considered necessary for good anesthesia in any good surgical procedure, several peculiar to the specialty. It should have no detrimental effect on kidney function, particularly in patients suffering with secondary cardiovascular damage and embarrassed circulation. Inhalation anesthetics are, therefore, to be avoided particularly in prostatic hypertrophy. In renal surgery, paravertebral block is applicable in a fairly limited group of cases and is not useful in the majority of kidney operations. Until 1929, these two authorities used **spinal anesthesia**, particularly for operations upon the prostate and bladder. Following Jeck's report they began to use it in renal surgery. The contraindications to the method have gradually become fewer as they became more familiar with the technique and have gained greater experience in its application. Originally, they were reluctant to use it in patients with hypotension, but with the use of **ephedrine**, this contraindication has largely disappeared. In cases with marked hypertension the margin of safety is somewhat reduced, but by avoiding the use of ephedrine until after anesthesia has been induced and so reserving it to prevent too great a fall in pressure later, they have seldom found it necessary to turn to other methods on this account. At the present time they are using it in 80 per cent of their operative cases. They consider just two factors—the comfort and mental tranquility of the patient, and the prevention, as far as possible, of unpleasant and undesirable experiences during and after the operation. They give  $\frac{1}{4}$  gram (0.016 Gm.) of **morphine**  $\frac{1}{2}$  hour before the anesthesia is to commence and occasionally a small dose of **hyoscine**. Only occasionally do they use **barbiturates**. When the patient is returned to bed, in addition to the usual procedures, the foot of the

bed is kept elevated for 3 hours, and if possible, the patient's head is not allowed to be raised for 12 hours. The principal postoperative complication, occurring in 4.5 per cent of their cases, is *spinal headache*. They have found pulmonary complications very much less frequently.

**Epidural anesthesia** is nothing more nor less than a high caudal anesthetic. The reviewer first saw this anesthetic used in von Lichtenberg's Clinic in Berlin. An Italian surgeon also does most of this work under this form of anesthesia. The reviewer (E. Hess, *J. Urol.* 31:621 (May) 1934) observed 75 cases of epidural anesthesia in von Lichtenberg's Clinic and then gave it a trial in a series of cases in his own clinic. The technic is important and can easily be learned by anyone skilled in giving spinal anesthesia. The tray should be equipped with 2 20 c.c. Luer syringes, 2 not too sharp ordinary spinal needles, a fine needle for the epidermal wheal, 50 c.c. sterile **normal saline solution**, 50 c.c. of 1 per cent. freshly prepared **novocaine** solution. (This is the anesthetizing agent used by the writer. **Nupercaine** or other local anesthetic agents may be used.) Depending upon the area to be anesthetized, the needle is inserted as in spinal anesthesia, between any two vertebrae that are selected. Outside of the lower anesthesias for suprapubic and prostatic work, a great deal depends upon the position of the patient. The technic is, therefore, slightly different in kidney and ureteral surgery than in suprapubic or prostatic surgery.

*Technic for Kidney Operations*—The patient is seated upon the side of the table with the back bowed, as for spinal anesthesia. The interspace between the eleventh and twelfth thoracic vertebrae is usually selected for kidney operations. A wheal is made in the skin with **novocaine** and a fine needle. A not too sharp spinal needle is then inserted and very carefully pushed toward the spinal canal. An attempt is made not to pierce the dura. As a rule, after a little experience, when the point of the needle goes through the intraspinous ligament and reaches the loose arcular tissue between the dura and the bony canal, a slight snap will be imparted to the thumb and finger, and the skilled operator will sense that the end of his needle is in the epidural space. However, it, upon pulling the obturator from the needle, the spinal fluid flows, no alarm need be felt if the needle has pierced the dura. It is withdrawn sufficiently, should this occur, for the spinal fluid to stop dripping. A Luer syringe filled with normal saline is then connected with the needle and injected. If resistance is met, the needle has been withdrawn too far and should again very slowly be pushed forward until the saline flows out of the syringe with very little, if any, pressure upon the plunger. The syringe should be next disconnected to see if spinal fluid again drips from the needle. The test as to whether the tip of the needle is in the epidural space is the lack of resistance to injection of the saline solution. Then 10 c.c. (2½ drams) of 1 per cent **novocaine solution** is slowly injected and the patient is allowed to lie with the head high on the side that is to be operated upon. Ten minutes is allowed to elapse. If at the end of 10 minutes there is no paralysis of the feet or legs and very little loss of skin sensation, one can be sure that the novocaine solution has not been injected into the spinal canal (a dry tap), when 20 c.c. (5 drams) of 1 per cent novocaine is again slowly injected with the patient lying as heretofore described, and a wait of another 10 minutes is allowed to elapse, at which time skin sensations are taken, both on the side to be operated and on the opposite side. After a final 10 minutes, the last 20 c.c. of 1 per cent solution is injected and the patient is allowed to remain in the same position for a subsequent 10 minutes. The patient is then ready to be operated upon. If, after the first 10 c.c. is injected, a spinal anesthesia is developed (this has never occurred in the writer's experience), operation may be performed without further injection with perfect safety. Ten cubic centimeters of a 1 per cent novocaine solution is

only about three-quarters of the dose for an ordinary spinal anesthesia and the margin of safety is practically 100 per cent.

#### Conclusions :

Epidural anesthesia should be a part of the armamentarium of every urological clinic.

It is an ideal anesthetic for operations upon the kidney and upper ureter where the general condition of the patient is such that other forms of anesthesia are contraindicated or risky.

It should not be used as a routine anesthetic

There have been, in the writers' experience, no postoperative anesthetic complications from its use.

A large percentage of the patients operated upon will complain of discomfort during the operation

It is perhaps the safest of all anesthetics to use.

In discussing this anesthetic, Jeck objects to it principally because of the length of time necessary to give it, and the uncertainty of getting good anesthesia after so much fuss and trouble.

**ANOMALIES OF KIDNEYS.**—The diagnosis of *horseshoe kidney* is being more frequently made, due principally to the fact that many cases have been carefully studied and recorded during the past few years.

A. P. Gorro (Urol and Cutan. Rev. 38:802 (Nov.) 1934) records a case which was diagnosed as a horseshoe kidney with calculi in the left renal pelvis. He shows that these kidneys are subject to the diseases that affect any normal kidney and, in addition, add their own symptomatology. Perhaps the most common symptom is the abdominal pain around or above the umbilicus. The majority of patients do not complain of pain and suffer only when they have some super-added pathological affection. Every renal tumor or rare radiographic shadow, particularly if accompanied by pain around the umbilicus, should be regarded as suspicious. He quotes Voorhave who says that the radiological symptoms of horseshoe kidney are.

- 1 Vertical position of the two kidneys
- 2 Symmetrical ptosis and approximation to the vertebral column
- 3 Visibility of the isthmus
- 4 Notch in the external border of the inferior pole

Marion and Papin consider abnormal situation of the two pelves, low and towards the median line, with an atypical pelvic image, and the ureter showing an atypical direction, as characteristics.

L. Solis-Cohen and S. Bruck (Pennsylvania M. J. 37:819 (July) 1934) report several interesting cases of horseshoe kidney with particular reference to congenital hydronephrosis. In discussing this article, G. L. Armitage, of Chester, Pa., emphasizes the fact that the existence of horseshoe kidney is no indication for treatment, and if discovered should be left alone unless there are some definite urological symptoms.

**POLYCYSTIC KIDNEY.**—The diagnosis and treatment of polycystic kidney disease has been particularly emphasized in the literature of the past year.



Most men agree that once the diagnosis of polycystic disease is made, surgical intervention is contraindicated, unless a catastrophe of some kind occurs. The *diagnosis* is becoming simpler as more and more of these cases are being seen.

Pain is a common symptom. It may be dull and aching in character, or it may be in the nature of renal colic, and usually is centered over one kidney. If there is a sudden hemorrhage, the pain may be severe. Fever and chills occur in cases harboring infection. It is difficult often to differentiate this condition from true renal neoplasms. There may be some gastrointestinal upset and asthenia. On physical examination an enlarged kidney can usually be palpated on one or both sides. Generally, if the left kidney is very large, a varicocele may be found. Hypertension is usually an early symptom. The outstanding features of the urinalysis are a fixation of the specific gravity and a mild albuminuria. The final diagnosis, however, depends upon good x-ray examination. The outstanding feature of the pyelogram of a polycystic kidney is a deformity of the pelvis due to pressure of the cysts. The calyces are elongated and bowed, and many of them are broadened. At times, some of them are abbreviated or entirely obliterated.

J. A. Lazarus (Urol. and Cutan. Rev. 38: 457 (July) 1934), in reviewing the diagnostic points, calls attention to the fact that *surgical intervention* may be required in cases complicated by stone, infection, hemorrhage, severe lumbar pain or impending uremia. The outstanding feature of the surgical procedure consists in the **puncture of the large cysts** with or without **nephrostomy**. **Nephrectomy** is only indicated in cases where the involved kidney is completely destroyed and the other kidney is capable of sustaining life. If one polycystic kidney is removed, the opposite side, if it has not already undergone cystic changes, will do so in a very short time after nephrectomy.

A few years ago the reviewer was obliged to do a nephrectomy for polycystic disease of the kidney, due to rupture of the kidney, with hemorrhage threatening to destroy life as a result of a very peculiar accident. The patient was driving an automobile and ran into a telegraph pole, pushing the steering wheel into his abdomen. He lived a year after the nephrectomy.

W. Walters and W. F. Braasch (Surg. Gynec. Obst. 58: 647 (Mar.) 1934) add also to the complications that may require surgical interference tuberculosis and neoplasm. **Surgical treatment** of polycystic kidney occurs frequently in their opinion. If the blood urea is 50 to 60 mg. or more, surgical treatment, except as an emergency measure, is contraindicated. In their opinion, the **Rovsing operation**, which was conceived for the purpose of removing pressure by the cysts on the remaining renal parenchyma, is still undetermined as to value. Theoretically, it has much in its favor.

An interesting series of cases is reported by C. Haines (Pennsylvania M. J. 37: 582 (Apr.) 1934), who considers the uncomplicated disease a medical condition. **Nephrectomy** was performed 6 times in a series of 21 cases and the **Rovsing's operation** twice. He considers **ethylene** the proper **anesthesia** to use in these cases. Rovsing's operation was without benefit in his experience. It is interesting to note that of the 6 patients who were nephrectomized, 1 died 4 days following operation, 3 remained well for 2 years, and all died before the third year. One patient lived 4 years, and 1 is still living after 7 years.

In calling attention to *pelvic kidneys*, a rather unusual anomaly, Wm. M. Coppridge (J Urol. 32:231 (Sept.) 1934) points out the fact that pain in the pelvis in women may be mistaken for disease of the generative organs. Infection is a common condition because of poor drainage, with hydronephrosis occurring in varying degrees. Occasionally, they interfere with gestation and delivery. Congenital malformations of the lower urinary and genital tracts may accompany the condition.

**RENAL CALCULUS.—Etiology.**—J. S. Joly (Urol. and Cutan. Rev. 38:1 (Jan.) 1934) concludes that human urine is a supersaturated solution. This is in direct consequence of the need in conserving water. It is only supersaturated in regard to the stone-forming salts. They are kept in solution by a special colloid mechanism. The first stage in stone formation is the precipitation of crystals in the urinary passages. The crystals thus thrown down are similar to those precipitated from a colloid solution. They are cemented together by a thin layer of colloid, which is also precipitated, and form minute rounded bodies composed of crystals arranged without form or order. These masses form the nuclei of the ordinary laminated calculi. The lamination portion of the stone is formed by a rhythmic deposit of colloid derived from the serum, and, therefore, foreign to the urine, coupled with a constant precipitation of the crystalloids. There is nothing specific in this method of stone formation. The chemical composition of the calculus depends on the nature of the salts in greatest excess. All calculi are, therefore, more or less mixed.

In an experimental study by C. C. Higgins (*Ibid.* p. 33) some very definite conclusions were formed. He was able by feeding Albino rats on a diet deficient in vitamin A to develop bladder and renal calculi. Bladder calculi thus produced disappeared upon the presentation of codliver oil to the animal. These stones were formed before infection was evident. As a result of these series of experiments, he is now investigating 5 patients with bilateral kidney stones and 1 patient with a stone in the lower calyx. One of the patients with bilateral calculi has been observed for 46 months, and no calculus has been passed until recently, since she has been taking a **high vitamin, low carbohydrate diet** for 4 months. X-ray studies show that many of the shadows present on previous examinations are now gone. The urine at present is loaded with sand, a finding that would seem to indicate that the stones are disintegrating. In one of the other patients who has had the same diet for 3 months, the calculi are definitely smaller, as shown by the x-rays. The stone in the lower calyx of the kidney has diminished considerably since the patient has been given the high vitamin, low carbohydrate diet. The other patients have not had the diet for a sufficient length of time to warrant drawing any definite conclusions. Likewise, the results in the few patients who have been subjected to this clinical test are too incomplete to make justifiable any definite conclusions regarding the efficacy of this treatment for urinary calculi. It is not improbable that in certain types of stones this may be the treatment of the future rather than surgery. It certainly is advantageous to place all cases who have been operated upon for stones upon a low carbohydrate and high vitamin diet on the theory that this régime may prevent the recurrence and a subsequent surgical procedure.

An enormous amount of work on the subject has been done by L D Keyser (J Urol 31:219 (Feb.) 1934). He discusses two factors in the production of renal calculi, metabolic perversions and specific infection. He believes positively that aseptic urinary concretions may be formed in consequence of metabolic errors, while stones composed chiefly of triple phosphate and the amorphous carbonate and phosphate of calcium are formed in alkaline urine probably the result of specific urea-splitting organisms. These are the varieties of calculi most frequent to recur and those which are seen most often in patients with stone-forming kidneys. Therapy directed toward the relief of urostasis and clearing up of infection is rational and attended with good results.

It is pointed out by J D Barney and E R Mintz (J A. M. A 103:741 (Sept 2) 1934) that *hyperparathyroidism* may have something to do with the formation of renal calculi. In a very excellent article they discuss the subject to date and make the statement that the realization that hyperparathyroidism will account for at least a part of the problem is a very important and encouraging finding.

F H Colby (Surg Gynec Obst 59:210 (Aug) 1934) discusses the same subject, making the statement that the fundamental problem in the consideration of urinary tract calculi is the prevention of recurrence. He concludes that *tumors of the parathyroid* cause metabolic disturbances, which result in a marked increase in the urinary output of calcium, a decrease in the output of phosphorus, and lead to the formation of stones in the urinary tract in many instances. While generalized osteitis fibrosa is frequently accompanied by urolithiasis, it is important to recognize the fact that stone formation occurs often in the urinary tract without any of the bone changes which characterize this disease, although tumors of the parathyroids are present and are the underlying cause of the stone formation. Unless the parathyroid tumor is removed stones will frequently recur.

**Treatment**—T Hryntschak (*Ibid* 58:103 (Jan) 1934) reports 15 cases of *bilateral nephrolithiasis*, 7 of which were operated upon on both sides in one stage and in the other 8 cases the calculi were removed in two stages. He believes that **operation** on both sides at one sitting has a great advantage, a fact which should be more generally recognized. He says that it is difficult to establish general rules as to the treatment in the presence of infection and branching stones in both kidneys. The course to take may depend upon various factors, such as the age of the patient, his general condition, the virulence of the infection, whether the patient suffers with colic or fever, and the social position of the patient must also be considered, as often it may be necessary to establish a kidney fistula, which the patient may have to endure for the remainder of his life. Often **nephrostomy** is the only possible operation in the presence of infection and coral stones, when, on account of the poor condition of the kidneys, nephrectomy of one is definitely contraindicated. Nephrostomy in such cases puts an end at least to the progressive destruction of the kidney. Removal, the relief of pressure in the renal cavities, and the abatement of infection often do much toward the recovery of the renal function. Removal of such stones without the institution of a permanent kidney fistula results in early recurrence of stone formation and the beneficial effects of the operation are completely lost.

Hryntschak believes that the removal of stones is contraindicated when they are aseptic and so small that it is more or less likely they will be spontaneously expelled; when a stone is fixed in a calyx and causes neither colic nor hemorrhage and causes no obstruction to the urinary flow; noninfected large calculi or coral stones, and where the calculi are so numerous that the chances of complete removal are almost *nil*. All other aseptic stones should be removed by operation, especially if their location and size are likely to damage the renal parenchyma. Where calculi are in infected urine, the general principle that such stones should be removed as soon as possible must be adhered to. This is especially true if the stones are of staphylococcic origin. The progressive destruction of renal parenchyma is almost a certainty if these stones are left to grow rapidly, as they usually do, and if operation is too late, danger of recurrence will be great.

H. P. Winsbury-White (Brit. J. Urol. 6: 142 (June) 1934) recalls that in many cases with lithiasis the condition has existed for a long time without causing symptoms. In his experience the majority of patients who suffer from colic either pass stones unaided, or do so after receiving instrumental assistance. In the vast majority of cases a plain radiogram suffices to establish the diagnosis. With him, *intravenous urography* is an established routine in all cases of suspicious stone in the upper urinary tract. He brings up the question as to whether or not **nephrectomy** should be done for calculus in one kidney and if it is, what are the chances of stone occurring in the opposite kidney? He answers this by saying that if a complete investigation of the urinary tract shows any evidence of disease in the opposite kidney, this evidence should weigh heavily against nephrectomy.

**HYDRONEPHROSIS.**—When the rôle that obstruction plays in the formation of hydronephrosis is understood, the symptoms of the disease are reasonably easy to understand.

F. Hinman (Surg. Gynec. Obst. 58: 356 (Feb. 15) 1934) describes the pathogenesis of the condition and makes the statement, after careful observation of his experimental findings, that the degree of structural repair and restoration of function which will follow removal of the obstruction will vary, not only with the extent of the injury which was produced, which is proportional to the period of obstruction and to the freedom from infection, but also with the degree and manner of functional stimulation. The gradually increasing excretory load which occurs with obstruction of the opposite kidney will effect a more permanent and greater structural repair than will a lesser stimulation, such as occurs when the opposite kidney has undergone compensatory hypertrophy, or a too sudden overload, as in the case of removal of the opposite kidney. An efficient compensatory mate diminishes and an insufficient kidney on the opposite side increases the potentiality of repair of hydronephrosis. He further states that the mechanical factor in the development of hydronephrotic atrophy is a back-flow of urine into the venous system, and whenever a back-flow fails to occur upon complete obstruction of the excretory duct, anuria develops and the pathological change of primary atrophy instead of hydronephrotic atrophy will result.

M. Grauhan (58 Tag. d. deutsch. Ges. f. Chir., Berlin, 1934) says that no premature conclusions should be drawn because of the size of the shadow in the pyelogram as to the severity and extent of hydronephrosis and the condition of the renal parenchyma. The important thing in considering the condition in either the unilateral or bilateral case is to determine the functional capacity of the kidney. The picture may be modified by changes in the renal parenchyma, especially by sclerosing inflammation. Pyogenic infection causes early injury to the vascular apparatus and scarring of the parenchyma, which renders the latter incapable of uniform atrophy or organic growth. The hydronephroses of the developmental period are to be considered as malformations resulting from disturbances in development and are only slightly amenable to correction.

Anomalies of the renal artery and the attendant mechanical injuries of the kidney have been the subject of much discussion during the last few years. J. R. Hand (Urol. and Cutan. Rev. 38:561 (Aug.) 1934) reports the opinions of Brewer, Eisendrath, Ekehorn, May, Braasch, McCarthy, Sanford, and Quinby on *hydronephrosis associated with anomalous vessels* and then reviews 6 cases of his own where this condition occurred. He calls attention to the fact that ligation of these anomalous vessels carries with them the possibility of cortical abscess developing in the infarcted area of the kidney. He believes that the end-results of **early operation** on the patient with anomalous vessels obstructing the ureteropelvic junction are highly satisfactory.

**Complications.**—Attention is called by K. Walker (Brit. J. Urol. 6:159 (June) 1934) to a very interesting case in which a large hydronephrotic kidney was complicated by *calculous disease* and a *squamous carcinoma*. He says that it is probable that the sequence of events in this kidney was first of all the development of a hydronephrosis, followed by a deposit of calculi in the cavities and, finally, through the chronic irritation these produced, the development of the cancer. The treatment of this condition is usually **surgical**.

**Treatment.**—C. P. Mathé and E. de la Peña (J. Urol. 31:1 (Jan.) 1934) call attention to the fact that operative failures are due to improper or insufficient correction of the obstructing lesion in the upper ureter and ureteropelvic junction, improper selection of the particular type of plastic repair in each individual case, and the lack of appreciation of certain technical points that are necessary for permanent relief of renal retention and hydronephrosis.

Early cases of hydronephrosis secondary to movable kidney, associated with angulation of the ureter due to fibrous bands or to its collapse and adhesion against the pelvic wall, can usually be relieved by **ureterolysis** and **nephropexy**. Hydronephrosis secondary to smaller aberrant vessels is best relieved by **ureterolysis**, **resection of the vessels** and **nephropexy**. In that due to obstruction by large vessels, **Young's method of resection of the pelvic sac** should be made in which the vessel's pressure is relieved or the ureter should be transplanted into a dependent portion of the pelvis away from the vessel. Lateral insertion of the ureter is best relieved by **lateral anastomosis** or **ureteropyeloneostomy**. Hydronephrosis due to early cases of large caliber stricture and valve formation of the ureteropelvic junction can be relieved by **longitudinal incision with transverse closure**. In advanced cases of stricture

formation resection of the sclerotic ureteropelvic junction, reimplantation of the ureter into the pelvis and temporary nephrostomy is the operation indicated. Calculus formation of the upper ureter and pelvis calls for the surgical correction of all mechanical etiological factors such as ptosis, ureteral stricture, obstructing aberrant blood-vessels, etc., as well as removal, of the stone itself. *Prophylaxis* against future stone formation consisting of **elimination of renal infection** and a régime based on chemical analysis of the stone should be carried out in all of these cases. In hydronephrosis due to sclerosing, infectious and traumatic perinephritis, **nephrolysis** and **ureterolysis** should be performed and the type of repair utilized which is based on nature and extent of the hydronephrotic sac.

**PERINEPHRITIC ABSCESS.**—This condition has always been difficult to diagnose. The most usual and persistent symptom is pain in the costovertebral angle on the side of the infection. This pain, as a rule, is fixed, boring, and becomes increasingly intense with the enlargement and formation of the abscess. The urological findings, as a rule, are essentially negative and the pyelograms will give little, if any, help. Given a patient with an elevation of temperature and increasingly rapid pulse, with or without chills, but with constant boring, severe pain in the costovertebral angle and the diagnosis of this condition should at least be suspected.

D P Bird (*Urol and Cutan Rev.* 38 318 (May) 1934) reports a case of an individual 28 years of age who was not acutely ill. His temperature was normal, the pulse slightly rapid. The abdomen was not rigid, but it was tender over the entire right side from the umbilicus to the vertebral column. No distention was present, although the right testicle was drawn upward toward the abdomen. The white count was 13,500. The pyelogram was normal. The following day he had considerable redness and induration over the kidney region. A lumbar incision was made and a perinephritic abscess was drained. The kidney was found to be normal. This condition later was found to be secondary to a general peritonitis, intestinal obstruction, resulting from a retrocecal appendix.

J H Shane and M Harris (*J Urol* 32 19 (July) 1934) review the roentgenograms in 40 cases in which operation for perinephritic abscess was performed in recent years at the Mayo Clinic. So that gas will not obscure the renal areas, an ounce (30 cc) of **castor oil** is given the evening before examination and an **enema** on the morning of examination. As a further adjunct, a compression band and inflated balloon are used on the ordinary Bucky diaphragm assembly. In 22 of their cases there was some associated pathological condition in the kidney on the involved side. The pathological condition usually found was pyonephrosis, with or without stones, cortical abscess, or some old inflammatory destructive process. The shadow on the psoas muscle frequently was obliterated. Scoliosis was found in 18 cases. The frequency with which obliteration of the shadow of the psoas muscle occurs on one or both sides, and the frequency with which some degree of scoliosis is found, diminish to some extent the clinical value of these data. Their conclusions as to the evidence presented by the x-rays is not in itself of diagnostic value.

**INFECTIONS OF KIDNEY.**—Infections of the kidney are always secondary. The symptoms are very often dependent upon the type of organism present. H. A. Fowler (*Urol. and Cutan. Rev.* 38: 594 (Aug.) 1934), in discussing *coccal infections* of the kidney, states that the infection by urea-splitting organisms, of which cocci are the most important in recurrence of stone, has been recognized. In these cases the importance of free ureteral drainage in combating all types of infection in the upper urinary tract is important. Ordinarily, the kidney is a self-irrigating organ and the pelvis and calyces are constantly flushed. However, this proper function requires free, unobstructive drainage of the ureter. Any degree of obstruction naturally interferes with this function. In the vast majority of these coccal infections drainage by means of the **ureteral catheter** is sufficient, while **intermittent catheterization** or the use of the **indwelling catheter** permits the direct application of various antiseptic solutions to the renal pelvis. Randall has recently suggested the topical application of 1 per cent **phosphoric acid** to the renal pelvis for the prevention of earthy phosphatic calculi. In lightly infected cases where stone is present, or without stone, if the infection is difficult to treat by ureteral catheterization, **pelviolithotomy** is a conservative and useful procedure because it is believed that **pyridium**, **serenium**, or **acriflavine** may be used as an effective internal antiseptic against the coccus group. They should be used routinely. He refers to the use of **neoarsphenamine** as giving good results. E. Hess (*The Urolog.* 1: 8 (Sept.) 1934) reports a case where a coccal infection was persistent even following operation but was immediately cured upon the exhibition of intravenous neoarsphenamine. In the occasional case where the disease is limited to one kidney, which has become seriously compromised by deep-seated inflammation, **nephrectomy** must be performed.

W. Darley and Wm. B. Draper (*J. A. M. A.* 102: 677 (Mar. 3) 1934) have had unusual success in certain types of *pyelitis* with the administration of **pituitary solution** because this drug augments the tone and peristalsis of pelvic and ureteral musculature. They report 16 cases of renal pain associated with symptoms of fever, nausea, frequency and dysuria, all of which were ameliorated by the injection of this drug. There is no question that this aids in the natural peristaltic drainage of the urinary tract.

Two cases of pyelonephritis due to the typhoid bacillus are reported by C. B. Huggins and N. W. Roome (*J. Urol.* 31: 587 (Apr.) 1934). Naturally, infections of this type have an interest both from the public health point of view and that of the urologist. Both of these cases were complicated by calculi and both were chronic urinary typhoid carriers. Both were cured by **nephrectomy**.

There is no doubt that a great many *pyelonephritic infections* in their various degrees of intensity are caused by organisms from the upper respiratory tract and it is a recognized fact where streptococcic and staphylococcic infections are identified in the urinary tract that a search should be made through the upper air passages for the primary focus of infection. Infected teeth, tonsils, and sinuses should be treated very often before any improvement will be noted in the general urological picture. It has been the experience of many men that the re-

moval of **badly infected tonsils** and **abscessed teeth** has often been sufficient treatment to clean up a persistent and aggravated pyelonephritis without the use of any other therapy.

A. J. Nedzel (*Ibid.* 31:685 (May) 1934) has done some experimental work with *nephritis* due to colds. He attributes the local disturbances in the blood supply of the kidneys, caused by exposure to cold, as a means of producing a favorable media for the growth of bacteria circulating in the blood stream. The streptococcus was often present in the upper respiratory tract, after exposure to cold, but may be absorbed into the circulation. It is during this exposure when the kidneys are suffering from circulatory disturbances, that the localization of the wandering microorganisms in the blood takes place. This localization produces inflammation which we call *nephritis*. The kidneys, without harm to themselves, excrete pathogenic bacteria. This proves that the presence of bacteria in the blood is not sufficient to produce *nephritides*. The tissues of the kidney must be ready to receive these migrated bacteria and present them with those conditions that will favor their growth and multiplication.

Other rare types of organisms attack the kidney. L. Kindall (*Urol and Cutan. Rev.* 38:569 (Aug.) 1934) reports a case of *actinomycosis* confined to a kidney of an 11-year-old boy. He recovered following **nephrectomy**. In the discussion of this particular case, Verne C. Hunt reported on a similar case and at that time there were only 11 cases of *actinomycosis* of the kidney in the literature. The preoperative diagnosis is rarely made, although the *actinomycoses* have been found in the urine preoperatively. The prognosis is notoriously poor and the report of a successful case serves as an excellent and valuable contribution.

**NEPHROPTOSIS.**—The diagnosis of *nephroptosis* is not ordinarily difficult. The symptoms are vague and unless a Dietl's crisis or an infection intervenes, there is little, if any, reason for treatment. Where the symptoms are such as to demand treatment, many men, as J. S. Rubin (*Urol and Cutan. Rev.* 38:558 (Aug.) 1934) and J. Salleras (*Ibid.* 38:84 (Feb.) 1934) say that they never fix a painless kidney, and J. U. Reaves (*Ibid.* 38:709 (Oct.) 1934) reports the technic for the operative correction of this condition. J. E. Strode (*J. Urol.* 32:171 (Aug.) 1934) uses strips of fascia lata, from 8 to 10 inches in length and  $\frac{3}{4}$  inch in breadth. This strip of fascia is then passed around the lower pole of the kidney beneath the capsule. The muscles are closed and the fascia brought up through them and tied under the subcutaneous tissues. He does not believe that he has had a sufficient number of cases, nor has the test of time made the operation one of proved merit.

On several occasions the reviewer has drawn attention to the fact that it is not necessary to suspend the kidney, but that if the **ureter** is thoroughly **loosened** and allowed to straighten, and the **kidney sympathectomized**, exactly the same results may be obtained regardless of the subsequent position of the kidney. Surgical suspension of the kidney without destruction of its nerve supply is almost sure to result disastrously, at least insofar as the comfort of the patient is concerned, and this operation should be approached with great care.



**NEPHROTOMY.**—In recent years the operation of **nephrostomy** has been given more and more attention. R. Gutierrez (J. Urol. 31:305 (Mar.) 1934) calls attention to the importance at times of making a preliminary nephrostomy before carrying out **nephrectomy** in selected cases of *pyonephrosis* in which the poor general condition of the patient does not warrant his exposure to the shock of the sudden removal of the much-diseased organ, or in which the surgeon finds at operation that the kidney is so bound down by adhesions and so greatly enlarged, with or without perinephritic suppuration, that a primary nephrectomy is contraindicated. Obviously, in renal surgery, when the kidney is functionless, primary nephrectomy is always the proper indication, provided the patient can bear it, and provided the other kidney has enough function to sustain life. There are certain cases in which nephrostomy as a preliminary drainage is not recommended, such as tuberculous pyonephrosis. There is no question but that many fatalities registered in the past could have been avoided by the application of this life-saving procedure.

G. C. Prather (*Ibid.* 32:578 (Dec.) 1934) says **nephrotomy** is necessary at times in order to remove large, branching *calculi* without sacrificing the kidney. There are other occasional cases in which **partial nephrectomy** seems feasible. Extensive cortical surgery of the kidney has rightfully commanded distinct respect if not fear, due principally to 4 factors, *i. e.*, (1) primary hemorrhage, (2) sepsis in the kidney cortex, (3) destruction of functioning tissue by the cortical incision or suture, (4) secondary hemorrhage.

To have as nearly a stone-free kidney as possible, rigid and absolute control of primary hemorrhage is necessary. This is accomplished by a pedicle clamp, the clamp being applied just tightly enough to produce hemostasis to prevent any damage to the vessels and the kidney. It is released for 20 to 40 seconds at the end of 8- to 10-minute periods during the surgical operation. Drainage is provided for this.

F. Hess (California and Western Med. 41:73 (Aug.) 1934) discusses the recent article by O. S. Lowsley and C. C. Bishop (Surg. Gynec. Obst. 57:494 (Oct.) 1934) and by H. Cabot and W. W. Holland (*Ibid.* 54:817 (May) 1932) and then goes on to say that a straight **nephrotomy** should not be done except in very rare instances. The hypothesis of Hinman is discussed as a point in the final decision in these cases. The most common indication for nephrotomy is a large *stag-horn calculus* in a badly damaged kidney, but in the vast majority of cases, regardless of its size or the number of its fragments, most calculi may be removed through a pyelotomy wound. A perfectly satisfactory pelvis has been observed to regenerate and be present after healing has taken place, even though it has been so badly damaged after operation that repair seemed impossible. In most cases with a good kidney on the opposite side, **nephrectomy** would be the procedure of choice. Small **nephrotomies** for small stones in dependent calyces may be at times a procedure of choice, but in these cases, if the parenchyma of the kidney is fairly good, the dependent portion of the kidney might be better treated by **heminephrectomy** with removal of the sacculization than by nephrotomy with only removal of the stone. Where nephrotomy must be done, the technic of Lowsley in tying a nephrotomized kidney together with large, broad

strips of catgut rather than using through and through sutures is recommended because it does not further add to the parenchymal damage sure to occur with the through and through sutures.

**PYURIA IN CHILDREN.**—M. F. Campbell (J. Urol. 31:205 (Feb.) 1934) calls attention to persistent pyuria in juveniles and emphasizes the fact that even though the pus has been cleared out of the urine by medical means or by the ketogenic diet, all of these children should be cystoscoped to ascertain, if possible, where and what the lesion may be. He calls attention to the fact that young children will stand major urological surgery better than their elders. The diagnosis can only be made by complete urological examination, treatment frequently requiring radical surgical attack. He also emphasizes the importance of the removal of foci of infection.

**PROSTATE.—ANESTHESIA.**—The proper anesthesia in prostatic surgery has always been a problem. Sacral, low spinal, and other forms of anesthesia have been tried with much success. W. N. Wishard, H. G. Hamer, and H. O. Mertz (J. A. M. A. 102:32 (Jan 6) 1934) discuss *transurethral prostatectomy* under *infiltration anesthesia* through the resectoscope sheath. They use a long needle which is thrust into the lobe of the prostate through the urethra and inject the anesthetic solution directly in and around the prostatic hypertrophy. They have done 33 resections under this type of anesthesia. The effects lasted 90 minutes in one case. The majority experienced only slight discomfort. In only one case was it necessary to administer gas because of insufficient anesthesia. The amount of tissue removed at each resection varied from 1 to 20 grams. The chief field of usefulness lies in obviating the immediate danger of inhalation, spinal or sacral anesthetics in certain bad risk patients.

**INFECTION OF PROSTATE.**—The prostate gland has always been a source of chronic infections. The most usual route, of course, is an ascending infection with the gonococcus, but it is also perfectly possible to have a non-specific prostatitis. This probably occurs more frequently than is ordinarily believed.

R. L. Smith (Urol and Cutan Rev 38:469 (July) 1934) says in the desire to arrive at a solution of the cause of nonspecific *prostatitis* and *vesiculitis* many histories have been taken in detail. Most of the histories record a previous illness with prolonged fever, such as typhoid, pneumonia, or influenza. Is it not possible to believe that the fluids in the vesicles and prostate are decreased in volume and that some precipitation of the fluid may occur which interferes with drainage through the small ducts of the genital tract? If this is true, the delicate muscle surrounding the tubules may become atonic, pressure within the tube increase, and prostatitis occur. Zeigler's "Pathology" states that the causes of inflammation are not specific and any injurious agent may incite inflammation if, on the one hand, its action is sufficiently intense to cause disturbances of circulation in association with tissue degeneration, but, on the other hand, not so intense as to completely destroy the tissue and stop the circulation. Pain in the back and upper thighs, perineum, painful and frequent urination with bleeding, urethral discharge in which no gonococci are found, are the symptoms observed. Patients

are frequently seen who have been massaged repeatedly without relief of symptoms, after thorough **dilatation of the prostatic ducts** in the urethra by sounds, however, the gland is usually emptied with ease.

L. H. Baretz (*Ibid.* 38:703 (Oct.) 1934) R. E. Cumming (*Ibid.* 38:769 (Nov.) 1934) and J. B. Clark (*J. Urol.* 32:495 (Nov.) 1934) report cases in which *prostatic calculi* have been found and treated. This is not an uncommon condition. The symptoms are usually those of rectal discomfort, frequency, urgency and dysuria, or the symptoms may be completely absent. The differential diagnosis, of course, is carcinoma.

**SURGERY OF PROSTATE.**—That the transurethral attack upon the *hypertrophied prostate* and the *sclerotic bladder neck* is a surgical procedure that has won its spurs is undisputed; that this type of surgery should be done only by those trained is equally undisputed.

J R Caulk (*Surg Gynec Obst* 58.341 (Feb 15) 1934) states that the accumulated knowledge of the physiology and pathology of both the upper and lower urinary organs have substantially transformed urological practice. Conservatism has become the keynote of modern surgical attack in urology. *Transurethral surgery* offers much to the senile prostatic whose life is fast ebbing away and who is unfit by virtue of his declining years and uremia-racked constitution to withstand the exigencies of open operation. It has also added comfort to the individual who is handicapped by *prostatic obstruction* but who in all other respects is a healthy, valued citizen. The preoperative preparation of the patient for transurethral surgery demands the same meticulous care as do patients who are subjected to open operation and also the same vigilant postoperative attention, in order that the hoped for results may materialize. Experiments were made with the idea of checking the difference between the production of heat in the tissues in doing transurethral operations by the *high frequency cutting currents* and the *cautery punch*. Caulk concludes that high frequency currents generate heat in the tissues at points distantly removed from the actual site of burning, often times a degree exceeding the thermal death point of the tissue cells. The tissue heat generated by the cautery current never penetrates to such depths. The coagulation currents producing pronounced superficial necrosis result in much less intense tissue heat than the cutting currents of higher tension values. The cumulative effects of heat generated in the tissue may be partially combated by restriction of the time duration of repeated applications of the high frequency current not to retard unduly the normal blood flow through the prostate gland. He presents a cautery instrument which can be operated under direct vision and which will cut under water.

E. Hess (*Arch. Phys. Therapy* 15 284 (May) 1934) discusses the fundamental principles and results of *transurethral surgery*. He found that the complications were in order of their frequency, troublesome hemorrhage, which usually can be controlled by returning the patient to the operating room, inserting the sheath of the resectoscope and evacuating the blood clot by suction, rupture of the bladder, which requires suprapubic operation and drainage at once. Dribbling was found in a large percentage of patients for a short time after they were allowed out of bed. There has been in this series no permanent cases of dribbling.

The longest case of postoperative incontinence was in an elderly man of 74, who regained good control after 3 months. The advocates of the open operation claim that this procedure is to be preferred because all of the prostate is removed. In a large majority of cases this is not true. The **adenomatous hypertrophy** usually starts in the glands of the commissure in the posterior urethra and as this glandular tissue undergoes hyperplasia, it presses the true prostate out, so that it forms the capsule of the adenomatous hypertrophy. It has been demonstrated by Caulk and others that it is not necessary to remove all of the hypertrophied adenomatous prostate, but that it is essential to remove that part which causes the obstruction. Is it not far preferable to have a patient still carrying some pathologic material, who is practically clinically-free from symptoms and who can almost completely empty his bladder, alive and comfortable with a minimum of shock, than it is to have one completely relieved of all his symptoms, dead or crippled and uncomfortable?

*Transurethral prostatectomy* has not been adopted by the foreign surgeons as enthusiastically as it has been by the American operator S. H. Harris (Brit. J. Surg. 21. 434 (1934) reviews 371 prostatectomies performed by him in a 5-year period ending October, 1932. In 356 of these cases primary closure was done after the prostatectomy. Suprapubic drainage was left in only 15 instances. There were 10 deaths, a mortality of slightly less than 2.7 per cent. In only 3 of the cases of primary closure was reopening of the bladder necessary. In one of the latter, cystostomy was done on the seventh day on account of incomplete drainage due to a faulty catheter. In another, cystostomy and blood transfusion were necessitated by a severe hemorrhage occurring immediately after the prostatectomy. In the third, the tip of the catheter found its way through the bladder incision and on the seventh day the bladder was opened, the catheter readjusted, and the prevesical space drained. The essential features of the operation are immediate control of hemorrhage by suture, reformation of the prostatic urethra with obliteration of the prostatic cavity, and immediate closure of the bladder and abdominal wound. This immediate closure of the bladder is certainly being done more frequently than in the past.

H. H. Haynes (J. A. M. A. 103:174 (July 21) 1934) discusses his technique. After enucleation of the prostate, complete hemostasis is obtained and the prostatic fossa is obliterated with plain catgut. An ordinary catheter used for irrigating and distending the bladder is left in the urethra during the operation. Before the fossa is obliterated, the end of the small intake tube of the special drainage catheter is sutured with strong silk or linen to the tip of the catheter introduced before operation. The urethral catheter is now withdrawn by an assistant and the special catheter readily follows through the urethra. When the distal end of the drainage catheter is withdrawn, the assistant removes the intake tube from the main catheter through a small oval opening. The button flap is adjusted over the intake tube and fastened in position to prevent leakage of the return flow. The intake tube is then attached to the irrigating apparatus and the return flow tube connected to carry the return flow into a suitable receptacle. The irrigation is now turned on to demonstrate that the drainage catheter is functioning properly. After obliteration of the prostatic fossa and complete hemostasis, the

Pezzer tip of the drainage catheter is drawn snugly into position. The usual suture to obliterate the space of Retzius is now placed but not tied. After this, the bladder incision is closed completely with two rows of No. 0 chromic catgut. The first row of sutures should include all the muscularis but not the mucosa and is a continuous lock suture. This row is completely buried by a continuous right angle suture. The suture, previously placed to obliterate the space of Retzius, is then tied. This suture is of great importance both in obliterating the space of Retzius and in preventing tension on the bladder incision. The abdominal wound is closed in the usual manner except that several loops of catgut extending down to the bladder are placed in the lower angle of the incision for drainage of the prevesical space; these are removed on the third day. Continuous irrigation by the drop method is started before the bladder is completely closed and continued for 24 hours. On the second day irrigation is done every 4 hours, and after the second day, morning and evening. Heat is an important factor in the irrigation, but care must be used to avoid burning the patient. The drainage catheters have been removed from the seventh to tenth days. The advantages of this practice are continuous or intermittent return flow irrigation with any desired solution, better drainage, shorter hospitalization, no suture anchorage of the bladder to the abdominal wound, assistance from the Pezzer tip in obliterating prostatic fossa, and better anatomic and functional results.

**Vesical neck obstruction** is not altogether peculiarly a male disorder. Very little appears in the literature regarding the control of bladder neck in the female. E. H. Fite (*Urol. and Cutan. Rev.* 38:163 (Mar.) 1934) quotes Stevens, Hunter and Caulk and their work in the treatment of this condition in the female. Nesbit, Collings, Beer, Braasch and others, have treated cases with the *McCarthy resectoscope* with splendid results. The lesion is typically a different type extending across the posterior half of the internal urethral meatus and obscuring a part of the trigone. These cases all show inflammatory changes with fibrosis. In many of these cases the bladder neck sclerosis is responsible for the failure of many repair operations to relieve the symptoms of cystocele. Treatment consists of *excision of the bar*, just as in the male, by means of some type of vesical neck resector. Caulk uses his punch, Nesbit and Fite, the *McCarthy resectoscope*.

**URETER.—ANOMALIES.**—E. H. Fite (*Urol. and Cutan. Rev.* 38:464 (July) 1934) and R. E. Alt (*J. Urol.* 32:249 (Sept.) 1934), in two very comprehensive reports, discuss the embryology of ureteral anomalies. This naturally includes a discussion of renal anomalies. The diagnosis of this condition depends upon complete urological examination and cannot, as a rule, even be suspected unless one or more of the ureters open ectopically either in the urethra or the vagina. In the female, particularly, the diagnosis may be suspected by the fact that the patient constantly dribbles urine as if she had a vesicovaginal fistula but also empties her bladder perfectly normally and without a history of injury. Given such a history, this condition should be immediately suspected. The **treatment is surgical.**

**INJURIES.**—Various injuries to the ureter, either as a result of instrumental manipulation or injuries occurring during pelvic surgery, accompanied by ureteral ligation and various other pathological entities, may cause the attending surgeon to **reimplant** one or both **ureters** to the body wall, to another portion of the bladder, or into the intestine. The diagnosis of these injuries is usually suspected and the degree of the obstruction is ascertainable by careful urological diagnosis.

Wm. E. Stevens (J Urol. 31:741 (May) 1934), in a thorough study of the injuries to the ureters, comments that this is a serious complication resulting disastrously in a large percentage of cases, especially if not recognized during operation. The left ureter is more frequently injured *during pelvic surgery* than the right, incision being the most common type of injury. A ureterovaginal fistula is the most common sequela of ureteral injury. Although, as Wesson has demonstrated, a normal ureter is never perforated by an ordinary ureteral catheter, this accident may occur if the ureteral wall has been damaged by some preceding pathological condition. The use of wire stylets should be abandoned. Operation is not necessarily required following perforation or rupture of the ureter. In certain types of operations, such as hysterectomy for carcinoma, the removal of large pelvic growths, and when difficulty is anticipated because of adhesions or other abnormal conditions, the insertion of ureteral catheters before operation is a time-saving procedure, aiding in the detection of the ureters and serving as an insurance against injury of these important structures.

A case is reported by J. S. Cooper (Urol. and Cutan. Rev. 38:234 (Apr.) 1934) in which the right ureter had been ligated *during a hysterectomy*. No symptoms developed from this accident for a year. He notes that the pain developed, not in the affected kidney, but in the opposite side, which was normal, although it had been the site of infection 3 years before, and that **removal of the dead right kidney** not only relieved the bladder symptoms but stopped the pain in the left kidney as well.

In discussing traumatic *injuries* of the upper urinary tract *following instrumentation*, R. B. Henline (J. A. M. A. 102:182 (Jan. 20) 1934) reports 9 cases in which he believes the ureter was ruptured or punctured during a cystoscopic procedure, because of existing pathology, and believes that this is more common than is ordinarily suspected. Surgical intervention is not indicated unless urography shows extravasation. Excretion urography has a very marked place in the study of those cases in which injury to the ureter may have caused extravasation.

J. G. Bugbee (J. Urol. 32:439 (Nov.) 1934) warns concerning the possibility of the occlusion of both ureters as a result of the common use of *radium implants into the cervix* for the treatment of carcinoma. He has been obliged to nephrectomize 6 patients since 1930 following the irradiation of the cervix.

Several years ago, the reviewer was obliged to transplant, in a series of 6 cases, both ureters into the flank because of this same treatment. The ureter had been so thoroughly destroyed that only the upper third was transplantable. These patients lived an average of 1 year following the **implantation** and died

of sepsis. It is, indeed, fortunate if only one ureter becomes sufficiently sclerosed by this treatment. In that case, **nephrectomy** may be done with good results.

**TRANSPLANTATION OF URETERS.**—The literature at the present time is filled with splendid articles by various men on the proper method of transplanting the ureters into the rectosigmoid. This treatment is indicated in **exstrophy of the bladder, complete epispadias, vesicovaginal fistula,** and other lesions of the bladder and urethra causing incontinence of urine in cases in which the plastic method of closure cannot be applied.

W. Walters and Wm. F. Braasch (Am J Surg 23:255 (1934)) operated on a series of 25 cases with 1 death. The operation is a *modified Coffey procedure*. In a series of 42 cases of exstrophy of the bladder, operation was postponed or not recommended.

In a review of 145 patients with congenital **exstrophy of the bladder** at the Mayo Clinic reported by L. M. Randall and R. S. Hardwick (Surg Gynec Obst 58:1018 (June) 1934), 35 were females. Twenty-eight have undergone bilateral transplantation of the ureters into the sigmoid. It is interesting to note 5 of the 28 have married and 4 of these have borne children.

**URETERAL CALCULI.—Diagnosis.**—The subjective symptoms of stone in the ureter may be so mild and vague as not to leave any suspicion in the examiner's mind that he is dealing with this pathological entity, or they may be so severe as to be agonizing. The symptomatology will depend a great deal upon the size and shape of the stone, its location in the ureter, the degree of obstruction that it causes, whether it is aseptic or infected, whether it is impacted partially, completely, or is freely movable, and whether it is rough or smooth. The symptom which drives the ureter calculus case to the physician is usually pain and this pain may be so severe that the patient when seen may be in actual shock, or so vague that the pain may be considered due to some intra-abdominal condition. Usually, if the stone is arrested in the upper third of the ureter, the symptoms are renal or upper abdominal, and the pain with its reference may be interpreted as arising in a gall-bladder, gastric or duodenal lesion. In the lower ureter the pain of ureteral calculi has often been mistaken for that of appendicitis, diverticulitis, salpingitis, or ovarian and parovarian cysts twisted on their pedicles.

The reviewer has seen a case of mesenteric thrombosis diagnosed from the subjective symptomatology before examination as ureteral calculus. There may or may not be burning and frequency of urination. There may or may not be the signs and symptoms that go with a hydro- or pyonephrosis. There may or may not be blood or pus in the urine and hematuria, while a frequent symptom, this is by no means a pathognomonic one. The question of a *differential diagnosis* between stone in the ureter and intraabdominal lesions has been the subject of much discussion between abdominal surgeons and urologists for years. On the right side the differential diagnosis between acute appendicitis and stone in the ureter is of such magnitude that it requires special consideration. The reviewer believes, as do most of the urologically-minded men throughout the country, that when in doubt it is far better to remove a normal appendix than to let appendiceal disease go on to fulmination, with gangrene or rupture,

while waiting to make a cystoscopic and x-ray differential diagnosis. In a general way, it may be said that with stone in the ureter the pain is excruciating; that in stone in the ureter simulating appendicitis the pain is much more intense. It is referred in women to the vulva or the inner side of the thigh, and in men to the penis or testicle on the right side. It usually is accompanied by some disturbance in the normal act of micturition. There is more apt to be a chill than in appendicitis. The elevation of temperature is apt to be less typical and the pulse rate is not apt to be quite so influenced. Gastrointestinal disturbances such as nausea, vomiting, and constipation or diarrhea, often help to cloud the picture because of the intense sympathetic disturbance in calculous disease. Rigidity of the right rectus and a fixed point of tenderness over McBurney's point usually are absent. If an immediate plain x-ray is taken and shows no shadow suggestive of calculus, the picture is further complicated.

Wm N Taylor (J Urol. 32 93 (July) 1934) reports a case of huge ureteral calculus treated by operative removal and comments on a series of cases of giant ureteral calculi by several observers. He states that the symptomatology of this disease is striking for its complete absence, at times, as well as its vagueness and variability in most of the cases reviewed. Subjective symptoms, when present, were referable to the bladder, abdomen or kidney.

**Complications.**—The possibilities of *extravasation of urine* are discussed by G. S. Foulds and D. H. Varey (Brit. J. Urol. 6:27 (Mar.) 1934), who remark that there is no tract where it is so uncommon as that of the ureter. There can be no doubt that a stone passing down the lumen of the ureter in almost every instance causes some injury to the mucosa, as red blood cells are so generally seen in the urine. The damage is seldom of any moment, and reports of rupture due to calculus are uncommon. They had the opportunity of studying a case of rupture of the ureter associated with ureterolithiasis and a review of the literature showed it to be a rare condition. The physical findings are those of stone in the ureter plus a mass either in the loin, back or lower quadrant of the abdomen. It would appear, therefore, that when symptoms and physical findings of ureteral stone are encountered in which the patient appears to be more seriously ill than is usual, extravasation of the urine from the ureter should be considered. Where this has occurred, in most instances, physical findings will be helpful in making a diagnosis, and cystoscopic investigation will frequently yield definite confirmatory evidence. Extravasation of urine above a ureteral stone must also be borne in mind as a possible etiologic factor in perinephritic abscess.

**Treatment.**—The treatment of ureteral stone depends a great deal upon its size, shape, position, and whether it is smooth or rough. The pain of renal calculus may be very slight or it may be so severe as to completely shock the individual. It is usually foolish to temporize in the renal colic of stone with less than  $\frac{1}{2}$  grain (0.03 Gm.) of **morphine**. Smaller doses than this do not relieve the pain if it is severe. If the stone is causing a great deal of pain, the patient, of necessity, should be cystoscoped and the urograms carefully studied. Various **catheter** and **bougie** manipulations through the cystoscope may suffice to relieve the back pressure on the kidney and give relief. If the stone can be



passed, an **indwelling catheter** with the injection of **sterile olive oil** may be all that is necessary to cause a small stone to be expelled into the bladder.

V L Pauley (Urol and Cutan. Rev 38 201 (Mar ) 1934) reports 5 cases of ureteral calculi which became impacted in the pelvic portion of the ureter. His treatment consists of a **spinal anesthesia** and **vaginal manipulation**, fixing the stone with the finger in the vagina, and then grasping the stone through the cystoscopic forceps and **removing** it. The vast majority of small ureteral stones can be removed by nonoperative measures. **Simple catheter dilatation, incision, meatotomy** of the ureteral orifice, **spinal anesthesia** and **the dilatation of the ureter** with the **inflation of bags**, as described by Dourmashkin, may all be tried. If there is any danger of complete blockage of the ureter or the stone does not readily move and is not readily discharged by careful cystoscopic manipulation, then surgery must be considered. The usual operative procedure is an extraperitoneal approach with identification of the ureter, a simple incision over the stone, and **removal**.

W E Lower (*Ibid* 38 28 (Jan ) 1934) describes his *operative technic* very clearly. He states that having once located the stone, the ureter is surrounded above and below the stone by tenaculum forceps which compress the ureter only slightly. This prevents the stone from escaping by moving upward or downward in the ureter during the manipulation of removal. The ureter should not be seized with any form of crushing instruments which might produce a local necrosis and subsequent fistula or stricture. The ureter is displaced as little as possible and it is not stripped too closely, lest there be interference with the blood or nerve supply and production of necrosis locally. It is most important that the field be kept free from blood. A longitudinal incision is made over or above the stone and the stone pressed up to the opening, or if the stone be of good size, the incision may be made directly over it. If it has been present for some time and has produced a periureteritis, it is dangerous to try to separate the ureter from the vessels, for in so doing the iliac vein may be torn with severe hemorrhage. The reviewer always inserts a drainage tube down to the ureter, and generally about 1 or 2 cm below the opening in the ureter. If the surrounding tissue is not too much disturbed, any leak is sure to be drained adequately. Lower closes the ureter with interrupted ligatures.

It has been the reviewer's experience that this is not a necessary procedure. If the ureter is dropped back without closing the incision and a cigarette drain placed down near the ureteral injury, it is very unusual for either a stricture of the ureter or extravasation of the urine to occur.

**TUMORS OF URETER.—*Diagnosis.***—Tumors of the ureter may be benign or malignant. The subjective symptomatology will depend a great deal upon the location of the tumor and the amount of obstruction that it causes. The subjective symptoms may be those of ureteral stone, with the exception that usually the hemorrhage from a tumor in a tube, with the active peristalsis of this musculo-serous organ, is apt to be far greater than the hematuria in calculous disease or tuberculosis. The diagnosis of primary tumor of the ureter is being made much more frequently today than ever in the history of medicine, and this is due to the fact that urography has been developed to such a degree that a very

accurate estimate can be made by the urogram. Usually, there is a normal ureteral shadow below the tumor, a blocking out of the area of the ureter involved by the tumor, with dilatation of both the ureter and pelvis of the kidney above the tumor. The differential diagnosis, of course, is made almost exclusively by cystoscopy, pyelography, and experience.

H. S. Argue (Urol. and Cutan. Rev. 38:232 (Apr.) 1934) reports a case of primary benign tumor of the ureter diagnosed preoperatively. His patient gave a history of 2 months' urinary frequency. She had some hematuria. Upon cystoscopy the tumor could be visualized hanging from the right ureteral orifice and was fulgurated. Later the symptoms recurred and a pyeloureterogram gave a definite picture of the tumor in the lower third of the ureter. The treatment is complete **nephroureterectomy**.

Primary *carcinoma* of the ureter is not as uncommon as has been heretofore believed. The diagnosis is virtually the same as that of benign newgrowth.

W. W. Scott (Surg. Gynec. Obst. 58:215 (Feb. 1) 1934) states that, due to the tendency toward more frequent and careful necropsies and the marked progress in the technic of urological diagnosis, primary *carcinoma* of the ureter has been found with ever increasing frequency during recent years. As there has been a considerable difference of opinion as to just what constitutes a true case of primary carcinoma of the ureter, it seems advisable to state briefly the conditions met by all cases included in this report. It was necessary to make sure that there was no primary tumor located elsewhere in the genitourinary tract and it was also necessary to prove that these were not due to a metastasis or direct extension from some point outside of the urinary tract. The site of most of the primary tumors in this series shows that involvement of the lower third of the ureter took place in 57 per cent. Most of the people were beyond middle age. While it is seldom that x-ray examinations yield conclusive proof of a primary carcinoma of the ureter, the findings are sometimes quite suggestive and tend to support the accumulative evidence in favor of such a diagnosis. Metastases in advanced cases may be observed in the bony structure. A negative plate for stone, plus the absence of a characteristic scratch on the wax bulb tip following ureteral manipulation, practically eliminates the possibility of calculus. In those cases in which ureteral calculus and traumatic stricture have been ruled out, a pyelogram, obtained by either the retrograde or intravenous method, showing a partially obstructed ureter with dilatation above the point of obstruction and an enlarged kidney pelvis with no filling defects of the type seen in primary carcinoma of the renal pelvis or parenchyma, suggests the possibility of primary carcinoma of the ureter, especially if there has been a story of recurrent hematuria and on cystoscopic examination blood flows copiously from the involved side. The value of intravenous pyelography in this disease has not as yet been determined.

**Treatment.**—Forty-five patients in this series were operated upon. Seventeen were given palliative treatment only, the diagnosis being positively made at autopsy. In a few instances deep **x-ray** and **radium** therapy were tried, but found to be of questionable value. In one case the x-rays eased the pain in the back for a while but failed to stop the process. The postoperative mortality in this series

was 27 per cent. Early diagnosis and **radical surgical removal** offer the greatest chance of cure.

S. Bergendal (Acta chir. Scandinav. 74: 179, 1934) reports a case of *sarcoma* of the left ureter in a man 28 years of age. The diagnosis was made prior to operation on the basis of the history and cystoscopic and x-ray examinations. Nephroureterectomy was done. Six months later the patient was returned to the hospital where he died. At autopsy, the ureteral stump was found to be free from tumor, but quite close to the stump there was a tumor which bulged into the iliac vein. There were metastases at the promontory, at the tracheal bifurcation, in the lungs, and in the left pleura. He believes that only by expert urological examination is it possible to make a correct diagnosis in the majority of cases. The treatment is surgical.

# Cancer

*by*

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**CANCER.—*Etiology.***—The carcinogenesis of certain tars has served as a stimulus for the performance of experiments in organic synthesis and analysis of the highest order of excellence. E. C. Dodds, in the Goulstonian Lectures for 1934 (*Lancet* 1: 931, 987 and 1048 (May 5, 12 and 19) 1934), has summarized briefly the work of the British group active in this phase of cancer etiology. It was generally assumed that tar produced cancer through chronic irritation, until numerous observations were made that not all irritative tars were capable of inducing malignant change. It was also common knowledge that tar contained, among other things, complex hydrocarbons. However, until Kennaway (1924) was able to produce a carcinogenic product by heating acetylene or isoprene in the presence of hydrogen, it was not known that the only organic constituents necessary to the carcinogenic elements in tar were carbon and hydrogen. Mayneord (1927) upon study of the fluorescent spectrum of these synthetic mixtures observed a spectrum similar to that cast by carcinogenic tar. Polycyclic aromatic hydrocarbons were definitely implicated a short time later by Hieger. Then, in 1932, came the work of Cook, Hewett, Hieger, Kennaway and Mayneord which definitely identified a series of compounds including 1:2:5:6 dibenzanthracene, 1:2 benzpyrene, and 5:6-cyclopento-1:2-benzthracene as being carcinogenic. Removal of the discovery of the structural formulæ for these carcinogenic compounds from the realm of academic interest has come with the elucidation of the structure of physiologically active compounds such as cholesterol, vitamin D and the sex hormones. The structural similarity is apparent. Furthermore, Cook has pointed out that processes entailed by the formation of these cancer-producing compounds from sterols and bile acids might well take place in the animal body.

The molecular resemblance of the carcinogenic hydrocarbons to the believed formula for the female hormone, estrin, prompted the trial of the former for esterogenic activity. Although 1:2:5:6 dibenzanthracene was found to be negative, 1:2 benzpyrene and 5:6-cyclopento-1:2-benzthracene were unmistakably capable of producing estrus.

The import of the work is obvious. Not only compounds highly similar in structure to the carcinogenic molecule have been recognized as normal body constituents, but these carcinogenic hydrocarbons are capable of producing a normal physiologic cycle in the animal body, namely, estrus.

In 1931, J. B. Murphy and E. Sturm demonstrated a factor in certain fowl tumors which had a definite inhibiting or neutralizing action on the transmitting agents of these tumors. The following year the nonspecific nature of this factor was proved by its ability to retard or prevent the growth of a mouse sarcoma. On these grounds the hypothesis was adopted that the balanced state and orderly growth of normal cells was maintained by the introduction of two forces, one which stimulates growth and the other which retards it (*J. Exper. Med.* 60: 293 (Sept.) 1934). A break in this balance might lead to uncontrolled growth. The authors reasoned that embryonic tissue, exhibiting as it does such high growth energy, should contain the highest concentration of the balancing factor to insure regulated growth. They struck upon an aqueous extract of desiccated mouse placenta and an aqueous extract of desiccated embryo skin as having a definite

retarding influence on the growth of two types of transplanted mouse carcinoma (Bashford 63; and mouse carcinoma 48). Control transplants were made in the same animals as the experimental transplants, the latter having been soaked for 30 minutes in the embryonic tissue extract. In tests involving 828 inoculations of tumor cells and the extracts, complete suppression of the growth occurred in from 55 to 71 per cent of instances, as compared with 21 to 27 per cent. in the controls. And in the absence of growth suppression there was almost always a retardation. Fresh embryonal extracts produced no such inhibition, nor did heterologous tissue extracts such as desiccated and fresh calf thymus, desiccated kidney and spleen of the rat and rabbit, early and term human placenta, and early cow, rabbit and hog placenta. However, the inhibiting action of heterologous tissue such as rat placenta and embryo skin and of rabbit placenta was quite definite. The failure of extracts of many of the above was explained by experiments with rabbit placenta showing that the inhibitor was not present until the beginning of the second third of pregnancy, and disappeared about 2 or 3 days before term. The negative results obtained through the injection of tissue extracts previous to the tumor transplants were taken as evidence against there being induced a subsequent general resistance to the tumor. The fact that no retardation was noted when placenta and embryo skin extracts were inoculated with mouse sarcoma No. 180 suggested a certain tissue specificity.

In a later paper (J. Exper. Med. 60: 305 (Sept.) 1934) the authors set about to test the inhibition factor on spontaneous or natural cancers derived from the animal's own tissues. Mammary tumors of mice served the purpose well because their wide use for investigation had given information on such points as the growth of autografts (grafts from one part to another of the same animal), local recurrence following surgical removal, spontaneous retrogression, and multiple foci of malignant change.

The recurrence rate of postoperatively recurring mouse mammary cancers is remarkably constant, averaging about 50 per cent. However, after radical mastectomy with the local injection of 0.05 to 0.2 c.c. of placental extract, only 6 per cent. recurred; and with embryo-skin extract, 25.9 per cent.

When a section from a spontaneous tumor is replanted in the same animal, the secondary tumor succeeds in growing in practically 95 per cent of instances. Murphy and Sturm removed spontaneous mouse mammary tumors, but before reimplanting them into the same animal one-half was soaked in placenta or embryo-skin extract and the other half in Ringer's solution. The autografts were made on opposite sides of the same animal. Ninety-five per cent of the control autografts grew, while only 32.3 per cent of the placental treated autografts grew, and 60.9 per cent of those treated with embryonic skin. There was an evident retardation noted in instances when inhibition was not complete.

Regression of spontaneous cancers in mice is less than 1 per cent. In a group of 142 primary tumors, 75 were treated with intraperitoneal injection of 1 c.c. of placental extract at 6 to 15 weekly intervals, and 67 were treated with embryonic skin extract. Over 20 per cent. of these tumors showed complete absorption, and 45 per cent. remained stationary or showed regression.

It is a well-known fact that about 35 per cent. of mice with spontaneous carcinoma develop secondary growths before death. Yet among 210 treated mice the rate of secondary tumors was only 3.3 per cent.

Histological studies on the grafts or unoperated tumors affected by the tissue extracts showed no striking structural change except the reduction or absence of mitotic figures after the onset of treatment.

The authors have proven the existence of a factor which will inhibit the growth of spontaneous or natural cancers made up of malignant cells derived

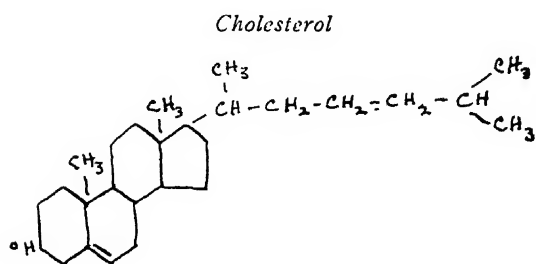


Fig 1

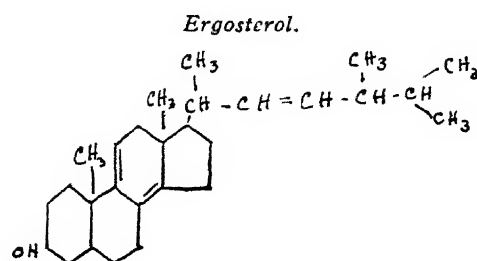


Fig 2

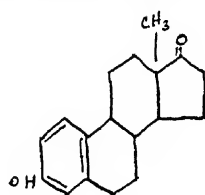
*Ketohydriory Estrin*

Fig. 3.

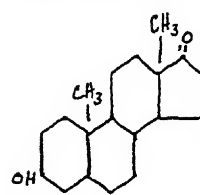
*Male Hormone*

Fig. 4.

1 2 5 6 Dibenanthracene

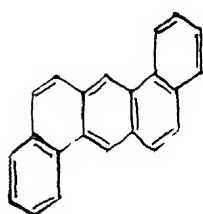


Fig 5

1 2 Benzpyrene

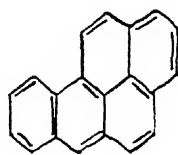


Fig 6

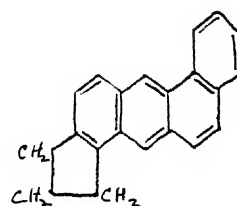
5 6-cyclo-Penteno-  
1 2-benzanthracene

Fig 7

(E. C. Dodds - Lancet)

from the animal's own tissue, and they are justified in the impression that the inhibitors affect directly the malignancy of the cell

L. I. Dublin (Bull. N. Y. Acad. Med. 8: 687 (Dec.) 1932) points out the clear relationship between cancer mortality and the factor of overweight from the Metropolitan Life Insurance Statistics. In men over 45 whose overweight was slight there was a 9 per cent. higher death rate from carcinoma than in men of average weight. This percentage death rate increase was 24 per cent. in men moderately overweight, and 30 per cent. in men greatly overweight. This raises



the question of these men being more liable to an internal metabolic change related to cancer, or of their being less amenable to curable procedures at hand

**Experimental Pathology.**—John W. Orr (Brit. J. Exper. Path. 15 73 (Apr.) 1934) pointed out the infrequent incidence of development of carcinoma in vascular areas and organs of the body as compared with those parts naturally hypovascular or hypovascular through circulatory interference. To test this observation experimentally, fibrous scar tissue was produced in the subcutaneous tissues of mice by the insertion of linen thread sutures which were subsequently removed and healing allowed to take place. Tar applications induced tumors more rapidly in these mice than in controls, and histological examination showed that the percentage of carcinoma at the twenty-first week was twice that in the controls

Local injection of vasoconstrictor drugs also produced an acceleration of tumor induction. The opinion was expressed that carcinogenic agents act upon cells which have been deprived of a fully adequate vascular supply

An attempt has been made by J. C. Mottram (*Ibid* 15 72 (Apr.) 1934) to determine the effect of cancer-producing substances on the chromosomal gene content of cells. He states that since the mutation hypothesis for cancer postulates that the cancer cell differs from the normal cell in its gene content, visible chromosomal disturbances may be taken as an assumption for disturbance in the microscopically invisible chromosomal components or genes. After subjecting growing bean roots to gamma irradiation, heat, carcinogenic tar solution, and a solution of gentian violet, a definite mitotic chromosomal deviation was noted in the anaphase consisting of fragmentation, and delayed migration of the chromosomal particles. These changes are not peculiar to cancer-producing agents, however, occurring, for instance, on exposure to acids, anesthetics, fertilization with foreign sperm, etc.

Either through the altered mode of utilization of dextrose in cancer tissue or through the altered affinity of such tissue for carbohydrate, H. E. Eggers (Arch. Path. 18 507 (Oct.) 1934) finds it conceivably possible to effect the cancer cell's selective intoxication by means of sugar compounds as carriers of toxic radicals. In the selection of such a toxic compound, he was limited to a compound of acids derived from sugar and a basic intoxicant radical. Lead gluconate, glycuronate, arabinonate, galactonate, glucoheptonate, d-mannonate, and rhamnohexonate were the toxic lead salts employed, and tetramethylarsonium gluconate, glycuronate, and galactonate were the arsenicals. The experimental data were determined on the growth of tumor transplants from the F. R. C. carcinoma and the R39 rat sarcoma, the toxic drugs being injected intravenously from 3 days after implantation upward. There was a general lack of uniform results with lead compounds. In an attempt to reduce the supply of other available carbohydrate for the tumor cells, high insulin dosage was used in conjunction with tetramethylarsonium salts. In the more malignant tumors more effective results were obtained with tetramethylarsonium compounds and insulin. When this treatment was used with the most malignant tumors studied, disappearance of the tumor transplants took place in 21 of 22 cases. The effectiveness of the toxic agents diminished rapidly fol-

lowing the third day after transplantation. In fact, their effectiveness 12 days after transplantation was practically *nil*.

B. Lucké (Am. J. Cancer 20: 352 (Feb.) 1934) has made a rather intensive study of a neoplastic disease in frogs (*Rana pipiens*) the neoplasms being characterized by locally destructive kidney tumors, epithelial in origin and gland-like in arrangement. In the majority of cases the picture was one of adenocarcinoma. The author found 158 tumors of this type and in a large proportion of these, prominent intranuclear inclusions were present which might be regarded as presumptive evidence of the activity of a filtrable virus. It was suggested that a virus caused the growth or invaded it secondarily.

**Diagnosis.**—From experience with 7000 biopsies for cancer at the New York State Cancer Institute, B. T. Simpson (South. M. J. 26: 48 (Jan.) 1933) has found no deleterious effects from the procedure. Those experienced in external cancer diagnosis in such lesions as cancer of the mouth, tongue and cheek have recognized *biopsy* as an essential to diagnosis. Simpson estimates clinical diagnosis of a carcinoma to be 70 per cent. correct at best, and macroscopic diagnosis of a tumor to be about 80 per cent. correct.

The difficulties of diagnosis and therapy in *malignant disease of the thyroid gland* have been discussed admirably by U. V. Portmann (Am J. Roentgenol 32: 508 (Oct ) 1934). He brings out the point that the acini of thyroid tissue have no basement membrane. Because of this, the thyroid capillaries and veins lying in close proximity to them are readily perforated. Emphasizing the difficulties of correct diagnosis from morphology alone, he cites Graham's review of 186 thyroids diagnosed as malignant adenoma. Graham was forced to throw out 108 cases, all but 4 of which were still alive. Of the 78 thyroids classified as malignant adenomas largely on account of blood-vessel invasion, 46 died of malignant disease. The possibility of error in the other direction was mentioned by Wilson (Mayo Clinic), who cited 97 cases of thyroid malignancy proven by recurrence or metastasis, 50 of which show no indication of malignancy before operation, and 23 of which were passed by the pathologist as nonmalignant. Malignant adenoma should be suspected in patients past middle age giving a long history of goiter, followed by sudden enlargement. The scirrhus type of thyroid carcinoma is usually characterized by a diffuse local growth. It has nearly 100 per cent mortality. Papillary carcinoma, however, is of slow local growth and reluctantly invades blood-vessels. Over half of these are favorable for cure. About 65 per cent of malignant adenomas are fatal, death usually resulting from vessel invasion and distant metastasis. When *malignant adenoma* was discovered after operation, **x-radiation** was begun and the adenomas were found quite radiosensitive. In *inoperable papillary carcinoma*, **radium implantations** were used, followed by **x-radiation**. This type was also found to be fairly radiosensitive.

M. Cutler (J A M A 101: 1217 (Oct 14) 1933) mentioned 4 benign *breast lesions simulating carcinoma*. They were plasma cell mastitis, traumatic fat necrosis, fibroadenoma, and ductal papilloma. Plasma cell mastitis is easily mistaken for cancer because of the development of a hard lump with axillary

adenopathy. Its sudden, often febrile onset and local tenderness should arouse suspicion which should be confirmed by subsequent biopsy

R. T. Frank (Proc. Soc. Exper. Biol. and Med. 31:1204 (June) 1934) has reported 2 cases of *carcinoma of the adrenal cortex* exhibiting a clinical syndrome similar to pituitary basophilic adenoma, namely, facial and trunk obesity, hirsutism, pig eyes, hypertension, amenorrhea or menstrual irregularity, pinkish skin striæ, rarefaction in the bones, polycythemia, acrocyanosis of extremities, and susceptibility to infection. Both showed a high female sex hormone secretion in the urine in the absence of a positive pregnancy reaction. The author points out that this biological urinary test to produce estrus in castrated mice may aid in the early diagnosis of adrenal cortical tumors, and perhaps may serve as a differentiating point from basophilic pituitary adenomas.

**Prognosis.**—The curability of *breast carcinoma* depends upon 3 factors of major importance, *viz*, the stage of the disease, the location of the tumor, and the thoroughness of the surgical procedure (E. I. Bartlett: West J. Surg. 41:243 (May) 1932). These conclusions were drawn from an analysis of 167 cases of radical breast amputation done 5 years or more ago. Of the group surviving operation and on whom follow-up data was available, 31 per cent were living and well at the end of 5 years. This figure is an honest one and probably represents fairly the curability of the disease in the average surgical clinic taking all cases as they come. Curability of carcinomas, classified according to location in the breast, was expressed in the following significant figures:

	5-year Cure
No axillary metastasis—outer hemisphere growth . .	77 per cent
No axillary metastasis—inner hemisphere growth ..	47 per cent
Axillary metastasis—outer hemisphere growth .	27 per cent
Axillary metastasis—inner hemisphere growth	4 per cent

Interesting data on the curability of genital carcinoma is contained in the report of J. Heyman from the Radiumhemmet (Deutsche med. Wchnschr. 58:367 (Mar. 4) 1932). During the 13 years preceding 1927, 1237 patients with *carcinoma of the cervix* applied to the Institute for treatment. In these, the absolute 5-year cure was 20 per cent. Almost all of these patients were treated by radium inserted into the uterus or vagina. During the last 3 years additional x-ray exposures were given the parametria. In 80 cases of *carcinoma of the corpus uteri*, the 5-year cure rate was 42.5 per cent. The author divided carcinoma of the ovary treated with x-rays into 4 classes:

	Survived 5 Years
24 hopelessly inoperable cases . . . .	9 per cent
36 operated upon, but not radically . .	22 per cent
28 patients, recurrence after operation . . . .	25 per cent
46 patients rayed prophylactically after operation.	54 per cent

There was no question of the value of postoperative prophylactic radiation.

**Treatment.**—An excellent summary of the results of therapy for *carcinoma of the skin* has been given by J. Nielsen at the Radium Institute at Copenhagen (Ugesk. f. læger 95:462 (Apr. 20) 1933). The report includes 800 cases treated from 1913 to 1932. The incidence of these lesions on the body in order of

frequency was as follows: nose, cheek, lower eyelid, temple, ear, inner canthus of eye, forehead, neck, hands, upper eyelid, trunk, upper lip, lower extremity, and upper extremity. Of 277 patients recently treated and followed, 139 were symptom-free for 5 years. The treatment was with **radium element packs**. The author agrees with Regaud in the dictum that "As the number of times treated increases, the number of chances for cure decreases." A massive dose first was advocated.

Attention was called to the high incidence on exposed body parts. The chief cause of death in head lesions was local extension to the cranium. Because of the radio-resistance of *scalp carcinoma*, **excision** was advocated, and in the case of *bone involvement*, **electrodesiccation**. Lesions of the *cheek*, *lips* and *nose* were favorable to **radiation** except in deep cartilage penetration. *Carcinoma of the ear* and *auricular canal* did not respond favorably to radium. Necrosis and perichondritis frequently resulted and metastasis to regional nodes was fairly early. **Radical surgery** should be applied in the beginning, or protracted fractional irradiation later.

In a rather comprehensive report R. H. Kennedy (Ann. Surg. 99:81 (Jan.) 1934) reviews the subject of *epithelioma of the lip* with particular reference to lymph node metastases. He states that for several years past treatment of epithelioma of the lip has been relegated more often to the radiologist. Early excision of the cervical lymph nodes has become correspondingly less common. **Radiation treatment of the neck** is often used accompanying or following the treatment of the local lesion. If enlarged nodes appear, some advise **block excision** or **partial excision** together with the insertion of **radium**. The author analyzes his cases with the idea of placing on record the findings when the initial treatment is exclusively surgical.

When not more than half the depth of the *lip* from the edge to the reflexion of the mucous membrane to the alveolus is involved, E. H. Molesworth (M. J. Australia 1:752 (June 9) 1934) employs the following procedure:

The lip is everted and fixed with strapping. After this, a dose of 700 "r" of the quality 120 K V constant potential, with 1 mm. of aluminum filter, is delivered to the inner surface of the lip over a semicircle, 1 c.c. of apparently normal mucous membrane being allowed to come into the beam. Of this, approximately 500 "r" survives at the opposite (skin) surface of the lip. The lip is then allowed to fall back into normal position and a similar dose is delivered to the skin surface over a similar area, a piece of lead rubber being placed between the lip and the teeth and alveolus. This brings the dose at each surface of 1200 "r" and the distribution throughout the lip is quite even. A dusky red reaction with some exudation occurs on the surface of the skin and there is frank erosion on the mucous surface. This begins about 8 days after irradiation and lasts for 3 weeks. Thereafter the improvement is rapid and at the end of 10 weeks the lip is well, with no remaining infiltration.

In the 50 cases observed by the author, in which he used the foregoing technique, the tumor has disappeared. There were 2 recurrences—marginal in each case and due to failure to expose a sufficiently wide margin of apparently healthy tissue. In only 1 case have the regional glands subsequently shown carcinomatous deposits. These 2 patients were operated on subsequently at an early stage with apparent success.

B. P. Widmann (Am. J. Roentgenol. 32:211 (Aug.) 1934) has reported 168 cases of *carcinoma of the lip* treated by **x-rays**, **electrodesiccation** and **radium**. In quoting a few of his sentences, it may be said that his experience has been in high accord with that of the reviewer. "Our clinical impressions warrant the inference that there is a tendency of all lip cancers to be resistant, and that too much significance should not be placed upon cellular differentiation for carcinoma of this particular anatomical site. Good results apparently depend upon adequate treatment of small lesions of short duration." Widmann, from his analysis, was able to emphasize the value of **prophylactic irradiation** in carcinoma of the lip. He found that with prophylactic irradiation of the neck, the subsequent development of cervical metastases occurred in 17 per cent. of 53 cases as against 51 per cent. of 72 cases without it. There was no evidence to indicate consistently affecting regression of metastatic nodes which were already present. On the basis of this experience, the **surgical removal of isolated movable metastases** seemed to be justified.

Treatment of *carcinoma of the tongue* at the Curie Institute of Paris, as outlined by T. Tailhefer (Rev. méd. franç. 14:785 (Nov.) 1933), consisted of implantation of **radium** element needles into the primary tumor, followed by routine **block dissection of the cervical nodes**. If the tumor approached the midline, both sides of the neck were dissected. *Inoperable nodes* were treated by **interstitial irradiation** preceded by the application of an external **radium-bearing collar**. Biopsy of the lesions was routine. The above type of treatment of tongue carcinoma coincides closely with that reported by E. S. Judd and J. R. Phillips (Proc. Staff Meet. Mayo Clin. 9:8 (Jan. 3) 1934). Here the tongue lesion was destroyed by **diathermy** and routine **neck dissection** was subsequently performed.

The management of *cancer of the mouth and the cervical lymphatics* is comprehensively considered by D. Quick (Am. J. Roentgenol. 31:366 (Mar.) 1934), who contends that the treatment of intraoral cancer must embrace 2 distinct, although not separate, problems, *i. e.*, the primary growth and the most unusual paths of metastatic dissemination. There is a tendency toward undue prominence, in a relative way, of technical details of primary growth treatment, in radiological literature. Associated factors in the care of the primary tumor and a definite plan for dealing with metastatic extensions to the neck are apt to be given slight consideration. These latter points are stressed. The term, *intraoral cancer*, is assumed to include clinically, epidermoid carcinoma of the oral mucosa, plus that of the maxillary antrum and structures of the tonsillar fossa. Growths of the nasal accessory sinuses, nasopharynx and hypopharynx are not included in this discussion. Anatomical and particularly histological considerations place them in a different clinical group, although many factors of cervical node metastases are common to both groups. Growths about the tonsillar fossa might well be claimed by either clinical group.

In the opinion of Quick, **external irradiation** at distance occupies the leading position and represents the first step in treatment of every case of intraoral cancer that is at all acceptable to treatment. A very few of the primary growths, from the group under consideration, may yield completely to this form of treatment.

alone. Usually, however, substantial but partial regression is all that is expected. Such aid permits of finishing the treatment with interstitial irradiation of lesser intensity, with greater accuracy, greater safety and less danger of secondary necrosis. When this advance is compared with the empiric and inefficient external therapy of even 10 years ago, it indicates something of the possibilities which the future holds for external radiation.

In the treatment of *intraoral cancer*, surface or contact applications of radium, no matter how heavily filtered, have no place. A high percentage of primary growths are dependent for completion of their therapy (after thorough external radiation) upon interstitial implantation in some form. **Radon seeds**, as permanent implants, represent the most efficient means of interstitial irradiation. Since Failla was able, in 1925, to seal emanation in gold capillary tubes, most of the objections to "seeds" have been overcome.

In one sense, the influence of histology on therapy is not as great within the mouth proper as in growths of the *nasopharynx* or *hypopharynx*. Within the past few years, intraoral radiation therapy has advanced from empiricism to a procedure of reasonable accuracy. The problem of tertiary syphilis as a complication is met with frequently in dealing with cancer of the mouth.

Quick contends that operative surgery has no place within the *mouth* for the direct treatment of cancer. Responsibility for control of growth should be vested in radiation. In order that radiation may be technically facilitated, and for certain definite associated complications, operative measures are indicated. For these, the cautery methods are preferable where feasible. **Surgical diathermy** affords greater adaptability than the older thermo-electric instruments.

The treatment of the *cervical lymph nodes*, metastatic or uninvolved, is regarded differently in various circles. By those taking a strictly surgical view, **neck dissection** takes precedence in importance, and frequently in sequence, to treatment of the primary growth. There are, however, numerous shortcomings of the routine in block dissection as applied to present day problems, but keeping in mind the fact that it was initiated before the radiation era.

In the *neck*, as in dealing with the primary growth, the histological picture is the outstanding guide to procedure. Complete differentiation may indicate **dissection following the external irradiation**, if the other indications for dissection are fulfilled. The wholly anaplastic tumor is one for external irradiation only. The intermediate histological picture contraindicates surgery but calls for implantation following external therapy.

Quick is convinced that narrowing of the limits for dissection and gradually increasing the scope of interstitial irradiation of metastatic nodes, after full external therapy, has conferred a larger benefit on a greater number of patients than did the former plan of free resort to dissection without adequate selection of cases.

In contradistinction to the views of Quick, regarding the value of surgery applied to lymph nodes of the neck, E. Fischel (Am J Surg 24:711 (Oct) 1934) gives the results of his work based upon an analysis of 66 lip cases and 112 cases of carcinoma of the buccal cavity and pharynx in a free cancer hospital. There is included for comparison a similar group of 47 private cases. All cases

were treated by bilateral suprahyoid resection of lymph nodes (for lip cases) or unilateral anterior and posterior triangle resection of lymph nodes (for mouth cases).

It is impossible to distinguish by palpation between hyperplastic and carcinomatous lymph nodes. Approximately 90 per cent of cases of carcinoma of the mouth have palpable cervical lymph nodes; 70 per cent. of the cases (including those with non-palpable nodes) in this study showed carcinoma in the lymph nodes.

The grade of the primary lesion either on *lip* or in the *buccal cavity* should not influence decision for or against **neck dissection**. According to Fischel, conclusive evidence that any method other than surgery is effective either in the prevention or the cure of cervical metastasis is lacking. In the cases studied, which showed proved carcinoma in the lymph nodes, in 33 per cent of the lip cases and 13.8 per cent of the mouth cases, the patients lived 5 years or more after operation. The **resection of lymph nodes** as an important part in the routine treatment of carcinoma of the lips and buccal cavity is to be strongly advocated.

In 1920, Coutard suggested repeated daily **x-ray** treatments of equal quantity and intensity given over a definite period of time (2 to 4 weeks) for *intraoral* and *pharyngeal cancer*. With such a technic, a massive total dosage was obtained at the expense of considerable local reaction such as external skin blistering and internal membranous mucositis, and some general radiation sickness. The advantage gained was the delivery of a lethal dose to an internal cancer by external irradiation approaching local and general limit of tolerance. H. E. Martin and R. F. McNattin (Am J Roentgenol 32 717 (Dec) 1934) have duplicated and slightly modified this technic in the treatment of 140 cases of carcinoma of the pharynx, tonsil and extrinsic larynx. They have delivered their dosage through cone-shaped metal tubes with a round orifice having a delivery portal of 7 to 10 cm. in diameter. Each side of the neck was irradiated on alternate days, receiving 400 r per dose. At the end of 20 treatments, the patient had received 4000 r (measured in air) on each side. The severity of the local reaction may be judged by the fact that gastrostomy was necessary in 3 cases and tracheotomy in 29 cases. With this technic, 29 per cent were free from disease from 1¾ to 2½ years after treatment. G. E. Pfahler and J. H. Vastine (Radiology 23 472 (Oct) 1934) published entirely comparable results to these, using a combination of radiological methods which may have produced less severe and uncomfortable reactions.

E. A. Graham (Am J Roentgenol 31 145 (Feb) 1934) has presented a brief but fertile resumé of *primary carcinoma of the bronchus or lung*. He stated that primary lung carcinoma constitutes 5 to 10 per cent of all types. He believes that practically all of these arise in a bronchus. Because of their early ulceration, bloody sputum, bronchial stenosis, bronchiectasis, atelectasis and lung abscess are frequent and early coincidental processes. Contrary to some conceptions, he found metastasis to take place early, the first evidence of disease having been from metastasis in 44 per cent of the cases. The most frequent metastatic sites were pleura, lung, mediastinal nodes, brain and long bones. Among the

local symptoms, chest pain, cough, dyspnea, sputum and hemoptysis were the most frequent. Diagnosis usually required bronchoscopic biopsy. Lipoidal instillation was a distinct aid in tumor localization. The course of the growth was variable, the duration of some extending over a number of months. This fact, in the author's opinion, accounted for the apparent success of some **x-ray** treatments. He cited 19 cases however, treated with high voltage x-rays which lived only an average of 5 months after onset of the treatment. The author, advocating **lobectomy** or **pneumectomy**, collected from the literature 6 cases of 1-year survivals following operation, and reported 1 case of his own done 6 months before and still well

M Cutler (*Ibid* 31:819 (June) 1934) has revived the discussion on treatment procedures for *bleeding nipple* and has added another form of treatment for the condition. His remarks have to do with bleeding from the nipple because of pathology within the breast and not in the nipple itself. He emphasizes that bleeding from the nipple in the presence of breast tumor should be regarded as evidencing carcinoma unless proven otherwise.

Bleeding in the absence of breast tumor offers diagnostic difficulty. In the author's experience, ductal carcinoma, which might cause bleeding and show no mass, is very rare. There are the following reasons for regarding duct papilloma, the most frequent origin of nipple bleeding, as precancerous:

- 1 Some breasts exhibiting bloody discharge ultimately become cancerous
- 2 Many years may be required for cancer to develop
- 3 In papillomas of other organs, carcinomas often develop (bladder frequently, colon usually)
- 4 Experimentally with tar cancer benign papilloma is apparently an early change in carcinomatous development
- 5 In the breast when carcinoma complicates papilloma the two occur in the same duct unit

It is well agreed that nipple bleeding even in the absence of tumor should not go untreated. The safest procedure is **breast excision**, particularly in women past 40. The author speaks of transillumination of the breast to locate the papilloma, then careful dissection of the area, thereby preserving the breast. As he remarks, such a procedure is fraught with difficulty and uncertainty. To meet the demands for treatment of the condition safely and adequately in younger women who wish the breast preserved, the author implanted **radium needles** into the papillomatous areas localized by transillumination (16 needles—1500 mg hr). Cutler reports 2 cases of 24 to 18 months cure respectively. He states that there is adequate proof that interstitial irradiation of *breast papillomata* results in destruction of the lesions and replacement with fibrosis. He is also sure that if early *carcinoma* is present, such treatment will be adequate to destroy it.

Regarding **x-ray supplementation to radical amputation** for *carcinoma of the breast*, U V Portmann (*Ibid* 31:46 (Jan) 1934) is convinced that the results obtained by intensive high voltage cross-fire irradiation are inferior to those secured by his older technic, *i e*, low intensity, low penetration. He is inclined to attribute the difference to environmental damage, presumably upon the structure deep in the chest, which followed the intensive treatment.



W. P. Healy and A. N. Arneson (*Ibid* 32:646 (Nov.) 1934) discussed methods for treatment of that type of *cervical carcinoma* in which the disease was no longer local in the uterine cervix. Patients with parametrial involvement comprise about 75 to 80 per cent of all cases of cervical carcinoma. They pointed out that with the usual methods of radium application to the cervix, the effective dosage was realized only at a maximum of 4 cm from the cervical canal. Since 1929, they have advocated preceding the local **radium** application with external **x-radiation** in all but early cases because it (1) diminished discharge and bleeding; (2) reduced the gross size of the primary lesion; (3) usually reduced constitutional and local reactions to subsequent radium application.

Although prolonged life and comfort have no doubt resulted from this method, they have failed to show any material increase in the total 5-year salvage over the local use of radium alone. They have therefore attempted to control more completely the parametrial disease by more intensive x-radiation. Their previous routine was 700 r to each of 4 fields. In order to obtain greater intensity of effective irradiation in the deep tissues, skin dosage must be increased and focal distance lengthened. In order to increase the skin dosage above 1 erythema, multiple exposures were given to each field. The following routine was used on 26 patients before the onset of local radium therapy. With a target distance of 70 cm, 200 r were given to an anterior and posterior portal for a total of 400 r daily, alternating right and left sides. Such a routine was applied over a 20 to 30-day period until each field had received 2000 r to 4000 r. No undue skin reaction was noted. Frequent cervical biopsies showed regression of the cervical growth. Temporary healing was noted grossly, but after the third week, proliferative activity was noted microscopically, even in the face of fibrosis produced by external irradiation. Following preliminary irradiation, a total of 4500 mc hours in 2 divided cervical applications was given. The authors hold some hope of effecting curability increase in parametrial involvement with this massive dose technique.

The late A. C. Heublein conceived the idea that in order to take advantage of varying times of mitosis, the total irradiation should be of low intensity so that it might be given homogeneously over the body and continuously over a long period of time. L. F. Craven and W. S. MacComb (*Ibid* 32:654 (Nov.) 1934) have described the operation of a 4-bed unit designed to give such continuous low intensity **x-radiation**. A Coolidge tube was placed at the ceiling of a 4-bed room, 5.4 meters from the near beds and 7.3 meters from the far ones. The factors for operation were 185 K. V., 3 ma., and 2 mm. copper filter. The beds were turned end for end twice a day. Between 1931 and 1933, 134 patients with generalized disease were treated. *Leukemias*, where extreme caution was observed, were given as high as 50 per cent S. E. D. over a 3-week period of more or less continuous irradiation to the entire body. The radioresistant group included epidermoid carcinoma, psammoma, carcinoma of the ovary, cancer of the prostate, cancer of the tonsil, cancer of the testis, melanoma and cancer of the breast. These cases did not do well. In the radiosensitive group it was concluded that treatment with **continuous rays at low intensity** given over a period of several days to 3 weeks was a valuable addition to the treatment of *leukemia*, *Hodgkin's disease*, *lymphosarcoma* and *multiple myeloma*.

# GYNECOLOGY AND OBSTETRICS

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**ABORTION,—THERAPEUTIC INDICATIONS.**—*Cardiac Disease.*—H. E. B. Pardee (J. A. M. A. 103: 1899 (Dec. 22) 1934) discusses the cardiac conditions indicating therapeutic abortion. He advocates dependence upon an estimation of cardiac functional capacity derived from the patient's history of past and present disability combined with the reaction to exercise at the time of observations. According to the results of this method cardiac patients are divided into 4 categories as follows:

*Class 1.*—Patients with heart disease who are able to undertake ordinary physical activity without discomfort, such as palpitation or dyspnea, and who perform the test exercise without unusual tachycardia or dyspnea.

*Class 2A.*—Patients whose ordinary activity is slightly limited because of the appearance of dyspnea, palpitation or fatigue, and who show somewhat excessive tachycardia and dyspnea after the test exercise.

*Class 2B.*—Patients whose activity is greatly limited because of the appearance of dyspnea or palpitation and who show marked tachycardia and dyspnea after the test exercise, or who are unable to complete it.

*Class 3.*—Patients whose activity is so limited as to make them unable to walk about without dyspnea or palpitation and who are so evidently dyspneic after such slight efforts as getting into and out of bed or walking across a room as to make any other exercise test unnecessary.

This method of rating the functional capacity of cardiac patients may be applied to pregnant women if the fact is borne in mind that during pregnancy a certain degree of limitation of ordinary activities because of fatigue, dyspnea and palpitation is a normal feature.

The occurrence of Class 2B cardiac insufficiency not improved by treatment in a patient during the fifth, sixth and seventh months of pregnancy is an indication for therapeutic abortion. An exception may be made (*a*) if the patient is anxious to have a child; (*b*) if she is able to have expert cardiac guidance during the remainder of the pregnancy, (*c*) if she is willing and financially able to cooperate with the physician as to restriction of activity; and (*d*) if she is willing to be delivered by Cesarean section before labor, should this become advisable.

The occurrence of 2B cardiac insufficiency not improved by treatment in a patient during the first 3 months of pregnancy is an even more imperative indication for abortion, for the patient must face the possibility of more marked cardiac insufficiency at the sixth or seventh month and, also, the possibility of miscarriage. Exceptions to this rule are very rare.

Patients first appearing with Class 3 cardiac insufficiency must be treated medically before the subsequent procedure is decided upon. In no case should operative procedures be undertaken until after a proper course of medical treatment.

Patients having auricular fibrillation and certain cases with congenital cardiac malformation must be considered as running a greater risk than others in the same functional class.

*Cardiorenal Disease.*—The phases of cardiovascular and renal disease indicating abortion are analyzed by W. W. Herrick (*Ibid.*, p. 1902). From a medical point of view the toxemias of pregnancy seem to fall into 2 groups. The first and smaller group includes the *nephritides*. These are examples of primary

nephritis and to these alone is the term "nephritis" strictly applicable. The feature of this group is prolonged and marked albuminuria with a tendency to anemia, edema and uremia. Hypertension is not obligatory. Cases of this kind do badly in pregnancy and usually require abortion when nephritic symptoms are manifest and do not yield to treatment. Repeated pregnancies are practically always unfortunate in outcome, leading to fetal death and acceleration of the downward course of the disease in the mother.

The larger group of toxemias seems to include the *eclampsias*, *preeclampsias* and the large number of milder disturbances variously classified under such terms as "*recurring toxemia*," "*nephritis*" and "*substandard kidney*." The dominant clinical feature of this group is hypertension. Nitrogen retention and uremia do not occur except rarely as the end-result of renal arteriosclerosis. Albuminuria is usually absent. When it is present, it is abrupt and late in appearance, variable in amount and, excepting in the hyperacute cases, is preceded by a considerable period of hypertension. During the acute phases of the toxemia, in the follow-up and at the necropsy in patients dying some years after the toxic pregnancy, the stigmas of hypertensive cardiovascular disease are found rather than those of nephritis.

In this group the problem of abortion is usually less urgent than in the nephritic group. In the acute eclamptic cases abortion is usually unwise, as it adds greatly to the maternal burden at a most critical time. Recovery with continuation of the pregnancy or the more frequent event of fetal death and spontaneous delivery, with relief of toxic symptoms, may be looked for in all except the 15 per cent of mothers who die in the acute attack. Except in particular cases with special features, conservative medical treatment is safest. In subsequent pregnancies the evidence of cardiovascular disease with hypertension must be sought. The incidence of this disorder in about 50 per cent of those having had eclampsia, preeclampsia and the milder types of hypertension in former pregnancies cannot be ignored.

In the less acute types the decision as to abortion may be made in more leisurely fashion. If hypertension appears early in pregnancy and increases despite treatment, abortion is indicated. When to hypertension are added albuminuria and edema not yielding to treatment, the same action is advisable. If viability of the fetus can be attained by delay, this may be risked in selected cases under careful supervision. The adverse effect on maternal health of the prolongation of pregnancy under these circumstances must always be borne in mind. There is no better recipe than this for the production of chronic vascular disease. Repeated pregnancies are to be discouraged excepting in the mild cases appearing late in pregnancy and usually with little or no albuminuria or edema. Some of these do not recur when reproduction is again attempted. However, when all is said, it must be emphasized that each case is an individual problem to be solved on its own merits.

**Tuberculosis.**—The indications for therapeutic abortion in tuberculosis are discussed by F. M. Pottenger (*Ibid*, p. 1907). The influence of the mechanical conditions of pregnancy and the puerperium on pulmonary tuberculosis are described. The change in intrathoracic mechanics during pregnancy seems to be

one of the most powerful forces which would be inclined to influence a pulmonary tuberculosis. It offers not only an explanation for the improvement that is witnessed in the later months, but also one for the increased activity that so often follows delivery. As pregnancy progresses and the uterus enlarges, the intra-abdominal pressure increases and pushes the diaphragm upward. This acts in much the same way as paralysis of the diaphragm following an operation on the phrenic nerve. By decreasing the size of the intrathoracic space, it aids the lungs, the volume of which is reduced by the tuberculous infiltration, in adjusting to this space which it must always fill; thus the pulmonary tissue is permitted to relax and conditions are brought about which favor healing. Unlike the phrenic operation, pregnancy does not paralyze the diaphragm, so it fails to remove the pull on the pulmonary tissue with its descent during inspiration and ceases to keep it elevated after parturition. In spite of this, however, the elevation alone, by lessening the intrathoracic space and maintaining the condition during the late months of pregnancy, may slow the activity in the pulmonary infection to such a degree as to bring about a temporary or even a permanent improvement.

Following delivery, on the other hand, the diaphragm, which has been elevated through the increased intraabdominal pressure, descends, allowing the lung tissue to expand. This not only takes away the protection afforded by the previous elevation, but brings about an extra hazard by causing increased respiratory and circulatory action in the dependent portions of the lungs; if the lung lesion is still active and discharging bacilli it furnishes an opportunity for new infection to take place through the secretions which may be drawn down into the bronchi. It further brings about conditions that favor the absorption of greater quantities of toxins.

This change in intrathoracic mechanics offers the most rational explanation of both the favorable influence that is noted during the time of the enlarging uterus and the ill-effects that follow delivery, for it is recognized that decreased motion and relaxation of lung tissue are of great value in healing and that increased motion and increased tension in lung tissue not only interfere with healing but may favor both increased activity and the formation of metastases.

In private practice among women who have been able to give themselves good care, the author always considers terminating the pregnancy if the disease is active and the condition has been discovered prior to the third month. The final decision, however, is determined very much by whether the patient will carry out the proper regimen of treatment, preferably in a sanatorium, both during the pregnancy and after delivery, and whether she will be relieved of the care of the child.

If proper care can be arranged and the patient apparently has good resistance, and provided the lesion is not extensive and is of the milder type, she may usually carry the child with safety. On the other hand, if the patient does not show evidence of good resistance and the tuberculous lesion is not of a mild type, and if the conditions for the mother during gestation and after confinement are not favorable, her safety will be best guarded by terminating the pregnancy at once.

The author's personal experience in terminating pregnancy has been far less favorable in those cases in which he intervened after the third month. The shock

is usually considerable, and the operation is quite often followed by increased activity in the lung. It seems better to give such a patient the best possible treatment, pneumothorax being used if necessary, and to allow her to go on to term under the care of a skillful obstetrician so as to throw the least possible strain on her during and after confinement. In a primipara, Cesarean section may now and then be the best way out. Under no circumstances should a mother with active tuberculosis nurse her child, and in case of open tuberculosis, the safety of the child demands immediate removal from contact with the mother.

There is also a type of patient in whom, although the tuberculous lesion may be quiescent, a pregnancy should be treated with the same degree of seriousness as the active cases just described, *i. e.*, patients who, on account of constitutional characteristics or because of bad environmental conditions, have been able to overcome a limited pulmonary tuberculosis only with great difficulty. Such patients are very apt to break down again under the strain of pregnancy, particularly if it occurs too soon following illness. The author always advises the avoidance of pregnancy until 2 years have elapsed after the tuberculosis has healed, yet he often permits a woman of good physiologic balance who has attained an arrestment of a tuberculosis more recently than that to complete a pregnancy should it occur. It is advisable, however, for her to be under close observation during the entire time of gestation and for a few months after delivery. Multiple pregnancies in women who have successfully overcome pulmonary tuberculosis are, in the writer's experience, inadvisable and are not unaccompanied by danger to the mother. One pregnancy is usually stood all right—in many instances two, but he has seen an increasing number of patients break down after a third or more. Particularly is this true in instances in which the pregnancies occur close together.

With the more recent hygienic methods of treating tuberculosis, there is noted a decrease in the number of complicating metastases, a reduction in serious symptoms and a very definite increase in the number of favorable results obtained, which fact has taken away from the tuberculous patient a certain amount of protection that was formerly thrown about him. Because it is observed that the body will stand extra demands better than it did when the patient was treated less carefully, there is a tendency to underrate the serious load that tuberculosis throws on the body and to subject the patient to strains that may be harmful even though endured.

This has produced a bolder attitude toward a complicating pregnancy, yet it must always be remembered that while tuberculosis is curable, in many cases even when advanced, it is cured with difficulty; and the prognosis is reduced by every complication that throws an extra burden on the patient.

No matter how slight the lesion, any patient can overcome a tuberculous infection best if spared all unnecessary strain. So, while a case may get by with an operation, a pregnancy or some other severe strain, the careful physician will shield his patient from all these complications when he possibly can.

**Toxemia and Eye Lesions.**—H. P. Wagener (*Ibid*, p 1910) discusses the conditions in the eye which are of more definite concern with reference to the question of therapeutic abortion, *i. e.*, those for which some type of toxemia of

pregnancy is definitely responsible. Included in this group are *optic neuritis*, *retrobulbar neuritis* and *hemorrhages in the retina* seen in association with pernicious vomiting, and *eclamptic amaurosis*, *angiospastic retinitis*, and *detachment of the retina*, which occur in the hypertensive toxemias of the later months of pregnancy.

It would seem that lesions of the retina and optic nerve in pernicious vomiting may be of more frequent occurrence than is generally assumed. It would be well to make more frequent ophthalmoscopic examinations in these cases to learn whether warning symptoms appear in the retina before toxemia reaches an incurable stage. It is well to emphasize that if in such cases and in cases of hypertensive toxemia examination is deferred until the patient has definite disturbance of vision, little can be done by the ophthalmologist except to give a serious prognosis.

The ocular lesion which has most aroused the combined interest of the obstetrician and ophthalmologist is the *retinitis* that occurs in association with hypertensive toxemia. This interest has centered in the diagnostic significance of the retinitis, especially with reference to the question of chronic nephritis, in its prognostic significance to the future health and vision of the mother, in its indications for termination of the existing pregnancy, and in its bearing on the advisability of future pregnancies.

From the standpoint of vision, the prognosis of retinitis of the toxemia of pregnancy usually is good. Most of the patients, even those who have had very diffuse retinitis, regain normal, or only slightly impaired, vision. It is true that the longer retinitis persists in its active phase, the more injury will be done to the retinal tissues and the less complete will be the return of function to the optic nerve and retina. The duration of the retinitis and the amount of edema of the optic disc and macula are of great importance to future vision. In the majority of cases, however, the end-results are surprisingly good.

The prognosis with respect to the future health of the mother is not so favorable, however. It is possible that spastic changes in the retinal arterioles may pass gradually into organic lesions without the appearance of retinitis. It is also possible that individual cotton-wool patches and hemorrhagic areas may appear in the retina without the presence of demonstrable organic lesions. It is true, however, that the development of cotton-wool patches and hemorrhages are at present the best available sign of the probable onset of the organic phase of arteriolar disease, and it seems quite improbable that diffuse edema of the retina and extensive exudation and hemorrhage can occur without spasm severe and prolonged enough to produce some permanent injury to the walls of the arterioles of the retina.

If a patient who has not had antepartum care enters the hospital in the latter weeks of pregnancy with symptoms of toxemia and diffuse retinitis, immediate interruption of pregnancy unquestionably is advisable, not only for the preservation of vision, but in the hope of minimizing the residual, permanent injury to the arteriolar system. Unfortunately, cases of this type are still seen. The majority of patients with toxemia of pregnancy, however, are seen nowadays before retinitis develops. In such cases it is the author's opinion that diffuse



retinitis should not be allowed to develop. In order to forestall its development, frequently repeated ophthalmoscopic examinations should be made to follow the development and course of the spastic lesions in the retinal arterioles. If, in spite of conservative management, the spastic lesions become more marked, termination of pregnancy should be urged at the first indication of localized hemorrhage or of exudation into the retina.

The beginning of retinitis marks the onset of irreparable organic changes in the arterioles and a delay of a few days may result in considerable injury, which could be avoided by prompt termination of pregnancy. If the fetus is of viable age, or if the toxemia and retinitis appear so early that it is obviously impossible to continue the pregnancy to the stage of viability, nothing evidently is to be gained by waiting. The most difficult problems for decision arise in cases in which the spastic lesions and retinitis develop at the stage of questionable viability of the fetus. When retinitis develops before viability, and pregnancy is allowed to continue for several weeks in the hope of obtaining a viable fetus, the chance of accomplishing this would seem to be too slight to justify the risk of increased injury to the vision and to the cardiovascular system of the mother.

The decision as to whether such a patient should become pregnant again must be based on the clinical estimation of the functional ability of the injured kidneys and vascular system to withstand the extra strain imposed by pregnancy. In most cases in which patients have had diffuse angiospastic retinitis, the residual vascular injury is sufficient to contraindicate further pregnancies. Patients who have had detachment of the retina without retinitis, however, may show little or no evidence of permanent vascular or renal injury and future pregnancies may be uncomplicated. The author has seen one such patient in whose case two later pregnancies were uneventful.

**Neurologic and Psychiatric Disease.**—( ) Cheney (*Ibid*, p 1914) believes that there is no specific neurologic or psychiatric disorder which is in itself and without exception an absolute indication for the interruption of pregnancy. He believes that not only the disease but its severity, its course, and the general condition of the pregnant woman have to be given consideration in the individual case. The problem would be rendered much easier if there were unanimity of opinion regarding conditions in the individual case which indicated abortion, but such is not the situation, and it would hardly be expected that any more unanimity exists in this problem than in many other problems in the practice of medicine.

There are, however, mental disturbances occurring in pregnancy which justify intervention when all other methods of treatment have failed; but it is very seldom that these indications must be approved unconditionally. This type of illness makes its appearance in abnormal reactions, in depressive moods, anxiety and fear, which are related to pregnancy. The pregnancy complex stands in the center of these manifestations. It goes on to an anxiety state, tendency to suicide, emotional outbursts, animosity toward the husband, neglect of duties and loss of weight. In these cases the loss of strength becomes so considerable that severe danger ensues, and then the interruption of the pregnancy becomes necessary in case other forms of treatment, such as psychotherapy and institutional treatment,

fail. However, careful, conscientious psychiatric observation is unconditionally necessary before a decision is made regarding the indications and, as a rule, should be done in a clinic. A suicide complex cannot be recognized *per se* as an indication for interruption of pregnancy insofar as a suicide fear is not a symptom of a psychotic condition justifying such a measure.

Experience shows that some women with severe advanced neurologic disorders may go through pregnancy and have healthy children.

Experience shows that some women suffering from severe mental diseases may pass through normal pregnancy and childbirth.

Experience shows that abortion does not necessarily prevent a recurrence of mental attacks or bring about recovery from attacks already existent. The general physical condition of the pregnant woman must be given careful consideration in a decision regarding the termination of pregnancy.

**ANESTHESIA IN OBSTETRICS.**—F. C. Irving, S. Berman and H. B. Nelson (Surg Gynec and Obst. 58:1 (Jan.) 1934) report an investigation at the Boston Lying-In Hospital into the amnesic, analgesic, and anesthetic properties in labor of drugs already in more or less common use, as well as other agents not at that time often employed for the same purpose.

In the study 860 patients were observed and 8 types of anesthesia were used, *i e*, pantopon and scopolamine, pantopon and rectal ether, pernocton, sodium amytal and scopolamine, pentobarbital and scopolamine, sodium amytal and rectal ether, pentobarbital and rectal ether, and pentobarbital and paraldehyde. There were 100 cases in each series, except in the group in which sodium amytal and scopolamine were employed, and this consisted of 160 cases. During the expulsive stage nitrous oxide and oxygen was given all patients, ether being added on the rare occasions when it was required.

One hundred patients were given **pantopon and scopolamine**. All cases in this series, as in the 7 others, were unselected, the drugs being administered to any patient entering the hospital who presented no major abnormality. The initial dose of pantopon was  $\frac{1}{3}$  grain (0.02 Gm). Later  $\frac{1}{150}$  grain (0.45 mg) of scopolamine was given 45 minutes later and the scopolamine was repeated in the same dosage as often as was necessary to dull the sensorium.

A modification of the so-called Gwathmey synergistic analgesia was next studied. An initial dose of  $\frac{1}{3}$  grain (0.02 Gm) of **pantopon** with 2 c c ( $\frac{1}{2}$  dram) of 50 per cent **magnesium sulphate solution**, was administered. Twenty minutes later 2 c c ( $\frac{1}{2}$  dram) of magnesium sulphate solution was given without the morphine. In 20 minutes to 1 hour the usual dose of **rectal ether, quinine, and olive oil** was given by rectum and accompanied by another intramuscular injection of 2 c c ( $\frac{1}{2}$  dram) of magnesium sulphate solution. The rectal ether was repeated every 3 to 4 hours if necessary.

**Pernocton** is administered intravenously. Since, if it escapes into the tissues, it may produce necrosis, it should be administered only by a physician. The dose employed was 1 c c (16 minims) per 30 pounds (14 kg) of body weight, given at the rate of 1 c c every 2 minutes. The average dose was from 4 to 6 c c (1

to  $1\frac{1}{2}$  drams). It was repeated if necessary at the end of 3 hours in half the original dose.

The study of **sodium amytal** and of **pentobarbital** in combination with **scopolamine** or **rectal ether** was next undertaken. The initial dose of sodium amytal by mouth was from 9 to 12 grains (0.58 to 0.77 Gm.), depending upon the weight of the patient. This drug was repeated 3 to 4 hours later in from 3 to 6 grain (0.2 to 0.4 Gm.) doses if indicated. Forty-five minutes after the initial dose of sodium amytal  $\frac{1}{100}$  to  $\frac{1}{150}$  grain (0.6 mg. to 0.45 mg.) of scopolamine was given subcutaneously and was repeated later as soon as the patient began to complain of pain.

**Pentobarbital and scopolamine**, the initial dose is from  $4\frac{1}{2}$  to 6 grains (0.3 to 0.4 Gm.) by mouth which may be increased if desired, and it is repeated according to the same indications as govern the use of sodium amytal.

Rectal ether was then combined with sodium amytal and with pentobarbital.

One hundred patients received pentobarbital and rectal ether.

The final group of patients were given pentobarbital and paraldehyde.

**Results.**—**Pantopon** and **scopolamine** in combination proved not to be satisfactory hypnotics, since only 34 per cent of patients had no memory of their labor. Only 33 per cent. of the infants born to mothers who had received these drugs breathed immediately after birth. There was also a prolongation of labor in primiparæ, the operative incidence was high, and the incidence of blood lost was the highest encountered in the study, being 25 per cent.

With **pantopon** and **rectal ether** there was only 18 per cent of complete amnesia, the lowest in the series. Sixteen per cent of the patients lost over 300 c.c. of blood, the second highest in the study. There was, however, a low incidence of excitement.

**Pernocton** is evanescent in its action and cannot be given until the end of the first stage of labor. It produces a low incidence of amnesia and considerable excitement.

**Sodium amytal** and **scopolamine** resulted in complete amnesia in 80 per cent of cases. No marked effect in delaying the initial respiration of the infants was noticed. There was, however, a fairly high incidence of restlessness, and the return to consciousness was prolonged.

**Pentobarbital** and **scopolamine** produced 86 per cent of complete amnesia, the highest in the study, and the greatest percentage of infants, 63, breathed immediately after birth. The operative incidence was low. The recovery after delivery was not lengthened. The frequency of excitement, however, was considerable, being 16.20 per cent. This is the only valid objection to the method.

With **sodium amytal** and **rectal ether** there was little restlessness, but the percentage of complete amnesia was only 72 per cent.

**Pentobarbital** and **rectal ether** was even less effective in producing amnesia, although the absence of excitement was similar.

**Pentobarbital** and **paraldehyde** produced a moderate incidence of complete amnesia. Twenty-four per cent of the patients, however, were sufficiently excited to require restraint.

In no case in any group was there noted an untoward effect upon mother or child.

The pulse, respirations, or systolic blood-pressure showed no characteristic variation during or immediately following labor in any group.

**Dial-Urethane.**—P. Brown (Surg. Gynec. Obst. 59:622 (Oct.) 1934) advocates the intravenous administration of dial-urethane for obstetric analgesia. The procedure is as follows:

The patient is told that she will feel relaxed and sleepy from the injection; a matter of some importance, because, otherwise, alarm may be experienced over the peculiar sensation. Four c c (1 dram) of the solution are drawn up into a 5 c c syringe and the needle thrust through the vein wall. Injection is made slowly, the patient being constantly questioned, and the injection discontinued when she no longer responds. In some cases, 2 c c ( $\frac{1}{2}$  dram) of the solution will suffice; in others, it may be necessary to inject the full 4 c c. (1 dram). If sound sleep does not occur between pain, a second injection of 2 c c. is given in 30 minutes. Further injections, each of 2 c c., may be given, but the writer has not exceeded a total of 8 c c (2 drams) in the course of any labor.

The author has used the dial-urethane solution in 56 patients and is definitely convinced that, used according to the method just described, it is the most satisfactory obstetrical analgesic.

In all cases requiring episiotomy or perineal repair, provision is made for administering ether by inhalation. A few cases require a small amount of ether; others do not.

Restlessness, so frequently a troublesome feature after amytal and apparently after pernocton and pentobarbital, has practically been absent in this series under dial-urethane. However, the importance of having the patient constantly under the observation of a responsible attendant until consciousness is fully recovered cannot be too strongly stressed.

There have been no stillbirths, nor any instances of serious respiratory depression in the child.

At any time if the patient is slow to recover or seems depressed, the condition may be corrected by intravenous injection of **coramine**, marketed in ampoules and stated to be a specific in all cases of barbiturate depression. The dose varies, but as much as 10 c c ( $2\frac{1}{2}$  drams) may be used at a single injection. The authors have not found it necessary to use the injections for the mothers, but always have the ampoules on the table for injection into the umbilical vein in case the infant manifests respiratory depression. The dial-urethane solution in ampoules seems to be a safe and effective obstetrical analgesic.

**Nembutal.**—L. Averett (Am J Obst and Gynec. 27:109 (Jan) 1934) discusses the use of nembutal and scopolamine analgesia in 160 cases of labor. The best results were obtained in the average case by the oral administration of 6 grains (0.4 Gm) of nembutal, made up into 4 capsules,  $1\frac{1}{2}$  grains each (0.1 Gm), at one time. Scopolamine hydrobromide,  $\frac{1}{100}$  gram (0.6 mg), is administered hypodermatically when labor is definitely established, with satisfactory uterine contractions at least every 5 minutes, and when the cervix is partially effaced and two fingers' dilated. The average duration of analgesia during labor

was 5½ hours. Only in 28 primiparous and 2 multiparous patients was additional medication administered, usually 3 grains (0.2 Gm.) of **nembutal** and ¼<sub>150</sub> grain (0.45 mg.) of **scopolamine**. The average duration of amnesia following labor was 2 hours. **Nitrous oxide and oxygen** was administered at the end of the second stage of labor in all cases.

The clinical effect of the drugs is drowsiness, followed in 15 to 30 minutes by profound sleep. Some patients awakened from time to time with the pains, others were only partially aroused, while a few did not move at all as pains appeared.

The frequency and severity of uterine contractions were not interfered with. The first stage of labor was unusually rapid in some cases, most likely due to the sudden relaxation and dilatation of the lower uterine segment. The second stage also progressed normally. There was no prolongation of the third stage noted. Postpartum hemorrhage occurred in only one case and necessitated uterine packing.

In 110 cases, the patients experienced complete amnesia after medication was administered. In 42 cases, the patients had some recollection of a few incidents during labor, but very little recollection of pain. In only 8 cases was complete failure experienced. These patients, all multiparas, were well advanced in labor upon admission to the hospital and were delivered in from 1 to 1½ hours after the medication was given.

There was no maternal or fetal mortality in the entire series and 152 babies either breathed or cried immediately after delivery, 8 required mild resuscitation, of these, 3 had been delivered by midforceps and one was a breech delivery with forceps used on the after-coming head.

C. B. Lull, in endorsing this form of anesthesia, reports that he completed a series of cases on the Vaux service at the Lying-In Hospital in which half the cases received a barbiturate with ether by bowel and the other half nembutal with scopolamine. There was a total of 265 cases in this series and Lull believes that the last 150 cases given nembutal and scopolamine were the most satisfactory. The nembutal was given by mouth in the approximate dose of 6 grains (0.4 Gm.) and the scopolamine in a dosage of ¼<sub>150</sub> or ¼<sub>200</sub> grain (0.45 to 0.3 mg.). He does not believe that the routine dosage should be the same for every patient, as he has found that the smaller dosage is sufficient in some cases, and also that in some cases it is not necessary to follow the nembutal with scopolamine.

He considers that there should be no routine analgesia administered to a woman in labor. Every patient should be given an analgesic, but it should be selected for every individual patient.

R. S. Hardwick and L. M. Randall (J. A. M. A. 102: 1558 (May 12) 1934) studied the *leukocyte content of the blood following* obstetric analgesia produced by *nembutal*. This drug given orally, has been proven to be an effective drug for producing analgesia during labor. It is generally considered that this drug has no observably deleterious effect on the infant and that the margin of safety for the mother with its use is great. Satisfactory analgesia can be obtained with no more than 10 grains (0.6 Gm.) of the drug given during the first stage of labor.

In an attempt to determine whether there was a deleterious effect on the leukocytes after the administration of normal doses of pentobarbital sodium for obstetric analgesia, studies were carried out on 59 parturient women; a control group of 10 patients who were not given this drug was also investigated.

Nothing in the behavior of the mother or child in any case in which pentobarbital sodium was administered indicated any deleterious effect. Studies of the blood from this group of patients give no evidence of a leukopenic condition with the amounts of pentobarbital sodium used.

This series of studies of leukocytic and differential counts indicates that the greatest leukocytosis occurs at the fifth hour postpartum. The number of leukocytes falls steadily to the fourth day, when the number of leukocytes per cubic millimeter of blood remains constant until the last examination on the tenth day.

**Infiltration.**—J P Greenhill (J. A. M. A 102:28 (Jan. 6) 1934) strongly advocates the use of infiltration anesthesia as opposed to general or spinal anesthesia for the following reasons:

- 1 There is practically no mortality due to this method
- 2 There are no pulmonary complications directly attributable to this procedure. It is of special importance in the delivery of women who have pulmonary disorders, such as tuberculosis, bronchitis, asthma and influenza. It is also an advantage in the delivery of women who have eclampsia and preeclampsia, because these patients are particularly susceptible to pneumonia
- 3 There are no local or general complications. There are only 3 possible sources of trouble. A needle may break during an injection. The second possible source of trouble is the injection of the solution directly into a vein. The third possible complication is an idiosyncrasy against the drug used. Greenhill always employs procaine hydrochloride (novocaine)
- 4 There is no bad effect on such vital organs as the liver, lungs, heart, circulatory apparatus and central nervous system
- 5 There is a striking reduction of bleeding in the field of operation, so that the amount of blood lost is almost negligible.
- 6 Gastrointestinal symptoms after operation are uncommon
7. Patients may take liquids and carbohydrates before, during, and after the operation
- 8 There is seldom need to hurry through an operation
- 9 Electrical apparatus, such as the cautery, may be used without fear of an explosion

(Obstetric operations that may be performed under infiltration anesthesia are the following:

- 1 Dilation and curettement for incomplete abortion, therapeutic abortion, hydatidiform mole, missed abortion and other reasons
- 2 Spontaneous delivery
- 3 Episiotomy and repair
- 4 Repair of childbirth lacerations, both recent and old
- 5 Low forceps delivery
- 6 Cesarean section, classic or cervical type, before or during active labor.
- 7 Porro's hysterectomy
- 8 Anterior vaginal hysterotomy (vaginal Cesarean section).
- 9 Sterilization, abdominal and vaginal.

Gynecologic operations that may readily be done under infiltration anesthesia are the following

- (A) Vaginal.
  1. Removal of Bartholin gland
  2. Vulvectomy.

3. Dilation and curettement.
4. Anterior colporrhaphy.
5. Posterior colporrhaphy.
6. Repair of third degree laceration.
7. Operations on the cervix, such as amputation or Sturmdorf operation
8. The Watkins-Wertheim transposition operation
9. Repair of vesicovaginal or rectovaginal fistula.
10. Vaginal hysterectomy.

(B) Abdominal.

1. Salpingectomy and oophorectomy.
2. Supracervical hysterectomy
3. Defundation
4. Suspension of uterus
5. Myomectomy.
6. Ectopic pregnancy.
7. Appendectomy.
8. Sympathectomy
9. Exploratory laparotomy

*Technic*—Usually obstetric patients are given a hypodermic of  $\frac{1}{4}$  grain (0.016 Gm) of **morphine** and  $\frac{1}{200}$  grain (0.3 mg) of **scopolamine** about 15 minutes before the infiltration of the local anesthetic is begun. Thus far Greenhill never saw any harm to the mother or to the baby from this procedure. The patients who are to have gynecologic operations are given  $\frac{1}{4}$  grain (0.016 Gm) of morphine and  $\frac{1}{200}$  grain (0.3 mg) of scopolamine 75 minutes before and  $\frac{1}{6}$  grain (0.01 Gm) of morphine and  $\frac{1}{200}$  grain (0.3 mg) of scopolamine 30 minutes before the operation.

For the local anesthetic, 0.5 per cent **procaine hydrochloride** is used, although 0.25 per cent is almost as effective. To this solution after sterilization, 2 drops of 1:1000 **epinephrine** is added for each ounce (30 cc). The amount of solution made up will depend on the type of operation to be performed. For small vaginal operations, such as episiotomy, repair of lacerations, dilation and curettement, plastic operations and low forceps operations, not more than 4 ounces (120 cc) is usually necessary. For laparotomies, including hysterectomy and Cesarean section, between 6 and 10 ounces (180 and 300 cc) must be used. It is advisable to make up a little more solution than is usually necessary.

Increased use of infiltration anesthesia will certainly reduce the incidence of postpartum and postoperative mortality and morbidity.

**CESAREAN SECTION.—INDICATIONS** The indications for abdominal Cesarean section are discussed by W. J. Stevens (Canad. M. A. J. 30:498 (May) 1934) from the standpoint of

1. Cephalopelvic disproportion
2. The hemorrhages of late pregnancy
3. The toxemias of late pregnancy
4. Systematic diseases complicating pregnancy
5. Previous Cesarean section

**Cephalo-Pelvic Disproportion.**—Contracted pelvis is the indication in 60 per cent of cases. Careful prenatal investigation is essential to determine the degree of disproportion which justifies Cesarean section. This investigation includes pelvic measurements, x-ray examination, Muller's test under anesthesia, digital examination, and the fitting of the fetal head to the pelvis. The obstetrical history of the patient's mother and the size of the paternal head are also considered. The operation may be considered as definitely indicated when the head

fails to enter by the Müller test; when the sacral promontory is readily reached; when the internal conjugate diameter is less than 8 cm. and the external conjugate less than 17.5 cm., or a transverse less than 8 cm., in slight degrees of contraction in elderly primigravidæ; and in cases with previous disastrous delivery.

Early induction of labor at the thirty-second week, if the head will enter the brim at that time, must seriously be considered in the case of a young primigravida.

A test of labor may be given in the borderline case, as disproportion may be overestimated, especially before the head has had an opportunity of moulding. A flat or high head may be due to uterine motor malfunction and not necessarily to disproportion. If, after an hour of severe pains at intervals of 5 minutes with full dilatation and ruptured membranes, there are signs of fetal or maternal distress, labor should be terminated vaginally or abdominally, otherwise the test of labor may constitute 6 to 12 hours of strong, active uterine contractions. Should the head still be floating, Cesarean section is definitely indicated.

**Hemorrhages of Late Pregnancy.**—In all primigravidæ and most multiparæ with a closed or slightly dilated cervix, central placenta previa is best treated by Cesarean section at or near term if the living baby and the mother are in good condition. Marginal placenta, lateral or low-attached, is also an indication for operation in the presence of pelvic contraction or a large baby.

In accidental hemorrhage the operation is often favored, especially in the case of acute complete placental separation. Blood and saline solution are transfused at the same time. Occasionally hysterectomy is necessary, especially when post-Cesarean hemorrhage is pronounced, persistent and not relieved by uterine stimulants and hot packs.

**Toxemias of Late Pregnancy.**—The operation is suitable in cases of pronounced preeclamptic conditions, fulminating nephritis at or near term with no indication of cervical effacement.

In eclampsia, Cesarean section is contraindicated, as the mortality is more than 25 per cent. There are 3 conditions for which the operation may be performed, *vide* (1) Failure to respond to at least 24 hours of active sedative elimination and attempts at the induction of premature labor when the baby is alive, with a disengaged presenting part and rigid cervix; (2) pronounced disproportion; (3) premature separation of the placenta during an eclamptic attack.

**Systemic Diseases Complicating Pregnancy.**—Operation may be necessary for the following conditions: Serious cardiac disease, advanced tuberculosis, diabetes, exophthalmic goiter, epilepsy, and such pelvic conditions as fibromyomata, ovarian tumors, bicornute uterus, rupture of the uterus, hernia of the uterus, contraction ring, osteoma, congenital obstructive malformations, varicosities of the vulva and vagina, previous operations, such as amputation of the cervix, uterine suspension, plastic operations; acute hydramnios; shoulder presentation with a live baby, early rupture of the membranes, especially if associated with pelvic complications, a neglected shoulder presentation when uterine rupture is feared, breech presentation with extended legs or with prolapse of the cord.



X-ray examination will reveal anomalies such as hydrocephalus or twins.

**Previous Cesarean Section.**—The danger of rupture is said to be 4 per cent after the classical operation. Pyrexia during convalescence is an indication of infection of the wound and a poor uterine scar. Previous Cesarean section for dystocia generally indicates the repetition of the operation. A subsequent pregnancy may be allowed a test of labor or be induced at the eighth month, careful watch being kept for threatened rupture if the previous operation was performed for antepartum hemorrhage, toxemia or a minor degree of contraction.

**OPERATION.**—The low cervical, or intraperitoneal retrovesical, operation is the one preferred, and described here. The usual preoperative investigations and treatment in cases for laparotomy and vaginal operations are followed. A douche is given the day previously, and again 3 hours before operation, 3 quarts (3000 c c) of a solution of **potassium permanganate**, in the strength of 1:5000, are used. The abdomen is painted with **tincture of iodine** in the strength of 5 per cent. **anesthesia** is induced and maintained with **gas, oxygen and ether**; the patient is placed in a modified Trendelenburg position.

**Advantages.**—The mortality for the low operation is less than half that of the classical one. The risk of peritonitis and other infections is greatly diminished, hemorrhage is reduced and the risk of subsequent hemorrhage is minimized. Postoperative discomforts and the chance of the subsequent formation of adhesions are lessened.

**CHORIONEPITHELIOMA.—Diagnosis.**—M. L. Leventhal and W. Saphir (J. A. M. A. 103:668 (Sept. 1) 1934) discuss the early diagnosis of this condition by the quantitative determination of anterior pituitary-like principle from the urine of pregnancy.

**Technic.**—The original mouse test is distinctly preferable for the exact quantitative determination of anterior pituitary-like substance in the urine. The original Aschheim-Zondek method was therefore used, with slight modification, as follows. The patient's morning urine specimen is diluted with physiologic solution of sodium chloride in fractional concentrations such as 1:10, 1:50, 1:100 and 1:1000. From 3 to 5 infantile white female mice, weighing from 6 to 8 Gm., are injected with a total of 3 c c of each of the dilutions within 100 hours. The animals are thereafter examined for the presence of vaginal cornification and ovarian stimulation, such as folliculation, hemorrhage and luteinization, as stated in a previous communication. On the assumption that a positive reaction would not be obtained with any of the dilutions but only with the undiluted native urine specimen, this would indicate that 3 c c of urine contains at least 1 mouse unit, or 1 liter of urine, a minimum of 333 mouse units. Accordingly, a positive reaction obtained with a 1:10 dilution would indicate a minimum excretion of 3330 mouse units per liter, a positive reaction with 1:100 dilution, an excretion of 33,300 mouse units, etc. It has been established that, in terms of mouse units, the excretion of the gonadotropic substance amounts to from 5 to 10 mouse units per liter of urine in both normal man and woman. This amount rises sharply to from 5000 to 20,000 mouse units in normal pregnancy, and any amount above 20,000 mouse units is indicative of the presence of a pathologic pregnancy, such as hydatid mole or chorion-epithelioma.

**CONTRACEPTION.—Safe Period.**—E. Novak (J. A. M. A. 102:452 (Feb. 10) 1934) analyzes the scientific data offered in support of the idea that women with menstrual cycles approximating the 4-weekly type are not likely to

conceive following exposures during a period up to 8 days after menstruation begins and in the 10 days preceding menstruation. To state the matter conversely, the maximum likelihood of conception is the period from the eighth or tenth to the eighteenth or twentieth day of the menstrual cycle, with the maximum at about the twelfth to fourteenth days. In women with irregular cycles the problem is more difficult and less certain. The new evidence, it would seem, offers practical advice not only to those who wish to avoid conception but also to those who wish to overcome sterility, since it sets forth for them the optimal time in relationship to conception.

W Shaw (*Brit. M. J.* 1:7 (Jan. 6) 1934) studied the ovaries in 36 cases in which women with a 28-day cycle were submitted to operation for various causes. In addition, he has collected 49 cases in which the uterus alone was removed. In 21 of the patients in whom the ovaries were examined, the uterus was studied histologically. In practically all of the cases examined for the presence of a ruptured follicle or a corpus luteum, the evidence was clear that ovulation occurs on the fourteenth day of the menstrual cycle.

Thus, there is being developed scientific evidence to warrant the possibility that this method for the prevention of conception or birth control is sufficiently accurate to be dependable and at the same time psychologically, socially, and esthetically sound.

An interesting editorial on this subject is presented in the *J. A. M. A.* 103:756 (Sept. 8) 1934. In a test of more than 100 so-called contraceptives undertaken by the Birth Control Clinic Research Bureau, New York, 45 were discovered to be unreliable. Today the marketing of devices, drugs and technics for the prevention of conception is in the realm of big business. Indeed, the marketing of books on the subject has also come to be an exceedingly profitable venture.

In a recent consideration of birth control as a business, Elizabeth H. Garrett credits the tremendous recent expansion to a court decision which affirmed that sales of materials for birth control were legal unless the seller was in complicity with drug stores to resell illegally. The court also said: "The intention to prevent a proper medical use of drugs or other articles merely because they are capable of illegal uses is not lightly to be ascribed to Congress." The decision was handed down in 1930. Immediately, the country began to be flooded with all sorts of material sent in circulars through the mails to doctors, druggists and the public. Advertisements for feminine hygiene began to appear in the most dignified periodicals. More recently the term "marriage hygiene" has been developed to point the use more specifically. Today there are hundreds of jellies, suppositories, rubber devices and systems sold for such purposes throughout the country, as well as many antiseptics that have about the same efficiency as water.

Considerable aid is afforded by the so-called Ogino-Knaus biologic law of nature, which deals with the establishment of the so-called safe period. The idea of a "safe period" goes back, of course, to the Mosaic laws, which, through their establishment of ritual cleansing and other processes for women, definitely indicated the period during which the woman was most likely to conceive.

It is claimed that the 5 days from the twelfth to the sixteenth day before a subsequent menstruation is the period of ovulation and that this period is the period during which fertilization is most likely. Within 24 hours after ovulation is completed the safe period probably begins. It is fairly well established that the fertilizing ability of the spermatozoa is within a 3-day period. In the vast majority of cases the human conception period is therefore within the 8 days from the twelfth to the nineteenth day before a subsequent menstruation.

Enough evidence has already been established to indicate that a strict observance of the method is insurance of sterility even beyond that associated with the employment of most of the contraceptive apparatus and medicaments. In the vast majority of cases it will, of course, be desirable for the family physician to instruct his patients as to the basis of this method of birth control and as to proper employment.

J. J. Latz ("The Rhythm of Sterility and Fertility in Women," Chicago, Latz Foundation, Chicago) states that he received only one complaint against the system for every 4000 books sold and in instances in which investigation was possible it was discovered that the employment of the method had not been intelligent. Smulders, in Holland, has made available records of many thousands of cases of successful practice of this method of birth control.

**DYSMENORRHEA.**—*Treatment*—A limited investigation of the value of **calcium** in the treatment of dysmenorrhea was undertaken by R. E. Boynton and E. C. Hartley (Am J Obst and Gynec 27:253 (Feb.) 1934) at the Students' Health Service of the University of Minnesota upon a group of undergraduates. Each had menstrual cramps severe enough to incapacitate her for one or more days each month. All of the patients were unmarried women, the mean age of the group being 20.3 years. Menstrual histories revealed no cases of menorrhagia, metrorrhagia, or oligomenorrhea.

Forty-nine cases of dysmenorrhea were treated. The therapy consisted of calcium gluconate alone, calcium gluconate with viosterol, alkaline mixture alone, or calcium gluconate and the alkaline mixture. Pelvic examinations were made on about one-half of the patients.

Of the 49 patients treated, 33 had either complete relief from abdominal pain, leg cramps, paresthesias, and nausea, or felt that they were definitely benefited, while 16 had no improvement.

The calcium was administered in the form of **calcium gluconate** by mouth. Sixty grains (4 Gm.) of calcium gluconate were given daily for 10 to 14 days before the onset of the menstrual period and continued through the first 2 days of the period. When **viosterol** was given with the calcium gluconate the dosage was 30 drops daily during the same period.

The alkaline mixture, which was used alone in a few cases and with calcium gluconate in other cases, consisted of equal parts of **magnesium carbonate** and **sodium bicarbonate**. The dosage used was 60 grains (4 Gm.) 3 times a day for 10 days before the onset of the menses.

The symptom of bruising easily seems to indicate, in cases of essential dysmenorrhea, that a more favorable response to calcium therapy may be expected than in cases without this symptom.

V. S. Counseller and W. M. Craig (*Ibid* 28 161 (Aug.) 1934) discuss the treatment of dysmenorrhea by **resection** of the **presacral sympathetic nerves**. Dysmenorrhea is divided into 2 types (1) Essential or primary dysmenorrhea, and (2) secondary dysmenorrhea, since it is associated with other demonstrable pelvic pathologic change, such as uterine myoma, endometriosis, salpingitis, ovarian tumors, and displacements. The latter is characterized during menstruation, by increased discomfort and other subjective symptoms, which usually subside when the period of flow is over. Surgical removal of the diseased organs and correction of malpositions of the uterus is all that is essential for satisfactory relief.

Primary dysmenorrhea, on the other hand, is not dependent on pelvic pathologic change, but may be associated with it. Primary dysmenorrhea has been one of the most difficult conditions which the gynecologist has had to treat; this is evidenced by the fact that many forms of treatment have been advocated.

At the Mayo Clinic, resection of the presacral nerve has been performed in 14 cases of dysmenorrhea. In all cases in which any associated pelvic pathologic condition was noted it was corrected at the same operation.

The results obtained from resection of the superior hypogastric plexus would indicate that the primary etiologic factor in dysmenorrhea is dysfunction of the pelvic sympathetic nervous system. When this dysfunction is corrected by resection the benefits are permanent, while the functions of normal menstruation and childbirth are not disturbed. If menstruation has been abnormal in amount and duration, there is a marked tendency for menstruation to become normal. Pregnancy has not occurred following sympathectomy in this series of cases, but a sufficient number of cases has been reported to determine that this function is not altered.

Resection of the presacral nerves is indicated in both groups, but only after medical and nonoperative measures have failed to give adequate relief. Other coexistent pathologic conditions should be surgically corrected at the same time sympathectomy is performed, since the results are far better. In this series almost complete relief was obtained in all cases.

According to Frank, certain groups of young women are particularly subject to this trouble—those of sedentary occupation, those who are harassed by the stress of life, or by overwork. Many of these patients respond to any show of interest, to anything which promises relief. Usually the effect is only transitory.

Frank feels that the profession at large should be seriously warned against contemplating operative procedure for the average case of dysmenorrhea, that perhaps in the course of many years an active gynecologist may be confronted with one case where the situation is so desperate—the patient has perhaps become a morphinist—that the choice is between a wrecked life and an operation which does not involve too much danger.

**ECTOPIC PREGNANCY.**—*Symptomatology.*—C. M. Echols (J. A. M. A 103:1686 (Dec. 1) 1934) records his observations in 103 cases of ectopic pregnancy seen in private practice. The ratio of ectopic pregnancies to births was 1 to 250 in Milwaukee County for the year 1933. The author is convinced that the increasing incidence of ectopic pregnancy is due to abortion rather than to gonorrhea.

Twenty-eight women of this series had had previous abdominal operations or abortions. Five of the women were either unmarried or widows. Previous total sterility was fairly common, but by far the largest group fell in the category of one-child sterility for a period of years preceding the ectopic pregnancy.

The commonest history was as follows. After a period had been missed for from 2 days to a week or more, flowing began and continued for weeks, accompanied by occasional lancinating pelvic pains. Many women in this flowing stage have been curetted, usually with a diagnosis of incomplete abortion. In no case in this series did the curettage produce more than a temporary check to the flow. Uterine bleeding in tubal pregnancies is much less profuse than in real abortions. About 20 per cent of the patients had no warning menorrhagia or uterine bleeding.

Tubal abortion, partial or complete, occurred about 4 times as often as rupture of the tubal wall. Correct diagnosis before operation was made in between 70 and 80 per cent of the cases. Hormone tests, such as the Aschheim-Zondek, have been disappointing. The extrauterine embryo is, usually, if not always, dead before vaginal bleeding begins. Since hormone tests become negative soon after the death of the embryo, they are apt to fail when they are needed most.

Patients with ruptured tubes can, and do, bleed to death. In the desperate cases, which constituted about 15 per cent of the series, Echols made it a rule to operate quickly if there was a breath of life in the patient, and to stimulate during and after operation. It is worse than a waste of time to mop the abdominal cavity dry. He removes only the large masses of clot and then the abdomen is filled with salt solution while the peritoneum is being closed.

During the operation, if time will permit, the author sucks out as much fluid blood as possible, filters it and introduces it into the patient's vein. As much as 1200 cc have been given in this way. Tubal abortion is a much less serious accident than tubal rupture. If it could be made certain which type were being dealt with, the condition could be allowed to improve before doing an immediate operation. These are the cases that present recurrent attacks of pain, bleeding and then recovery. It is when the clot can no longer hold the pregnancy in the tube that profuse fatal bleeding may occur. In the rupture of the tubal wall, however, there is no temporary stoppage of bleeding.

**Residual Tube In.**—I. C. Rubin (Am J Obst and Gynec 28:698 (Nov) 1934) discusses the status of the residual tube following ectopic pregnancy in relation to sterility and further pregnancy, based on a study of 90 patients. Sixteen were examined by uterotubal insufflation within 2 years after the ectopic pregnancy, and 74 later than 2 years. Eight patients had repeated ectopic pregnancy. Only 12 per cent. of the 90 tubes were normally patent; 43 per cent were completely obstructed, and 44 per cent. were partially obstructed. Of the 23

untreated patients who again became pregnant after the tubal pregnancy, 7 proved to have normal tubal patency; and of the 27 untreated patients who did not again become pregnant, only 6 had normal tubal patency

Of the 77 patients who desired again to become pregnant after a tubal pregnancy, 12 became pregnant after insufflation. Ten of the tubes showed some impairment of patency and function, and 2 were normal. Eight of these 12 patients had an intrauterine pregnancy, and 4 developed another tubal pregnancy. There appeared to be a definite relationship between the development of intrauterine and extrauterine gravidity on the one hand and the pressures encountered during the insufflation on the other. In general, the pressures approaching 100 mm. Hg at uterotubal insufflation were followed by uterine pregnancy. The higher pressures (150 to 200 mm Hg.), indicating marked strictures, were followed by tubal pregnancy. Insufflation repeated once or several times may improve the tubal status and favor normal pregnancy.

Intrauterine pregnancy occurs with sufficient frequency after an operation for tubal pregnancy to encourage conservation of the residual tube. It occurs in spite of impairment in tubal patency.

**Treatment.**—In the surgical treatment of ectopic pregnancy, a distinction should be made between multiparous and nulliparous women. For the latter, especially, the following surgical rationale suggests itself.

When the patient's condition is serious, as little as possible should be done other than to insure the safety of the patient. The uninvolved tube should not be disturbed, although it should always be inspected for the possibility of a coexistent tubal pregnancy. Inspection of the ovaries has similar importance. This rule applies to both parous and infertile women.

When the patient's condition is good, the uninvolved tube should be carefully scrutinized. If it is hopelessly diseased and the patient has borne a child, it should be removed. If only partially impaired, it should be left *in situ*, because intrauterine pregnancy occurs more often under such conditions than tubal pregnancy. The mere possibility of a second ectopic pregnancy is not an indication for salpingectomy. In any event, its pathologic status should be recorded as accurately as possible for the future.

Whenever possible, abnormal conditions should be corrected at operation. A **salpingostomy** or **freeing of adhesions**, or both, may be required.

In cases of *repeated ectopic pregnancy*, when the patient is anxious to have a child and is willing to risk a third ectopic pregnancy, a **partial salpingectomy** may be performed with a **plastic operation on the tube stump**. The alternative of removing the gestation sac by **simple incision and suture of the tube**, with or without **curettement of the tube**, may be borne in mind. The feasibility and value of this procedure await future experience.

The early diagnosis of unruptured tubal gestation will make conservative operations on the pregnant and nonpregnant tube safer and more feasible.

**GONORRHEA IN FEMALE.**—**Treatment.**—In a discussion of the treatment of gonorrhea in the female, E. D. Barringer (J. A. M. A. 103:1825

(Dec. 15) 1934) states that gonorrheal cases clinically fall into 3 groups: Acute, subacute and chronic, and the treatment will vary with these different stages.

1 In the *acute stage* the main indications are for absolute rest, lack of trauma, and treatment directed toward preventing the spread of the infection. Ill-advised douching and medication of the cervix in very acute cases may result in just the outcome which the physician is trying to prevent. It is debatable whether, in these very acute cases, **rest in bed**, with carefully ordered **general medical supervision**, and only **local cleansing of the external genitalia** do not lead to recovery as satisfactorily without local treatment.

However, in acute cases in which it is obvious that the infection is ascending, it is wise to give the patient, in addition to absolute rest, **mild heat** in the form of **medicated douches** under low pressure and the administration of a **solution of mild silver protein** by gentle application to the **cervix and urethra**. The greater degree of heat, 130° F (54.4° C) as given by the Elliott machine, seems unwise during the acute stage because of the softening and relaxation of the cervix, thereby opening up one of the natural barriers to the spread of infection.

2 In the *subacute stage* the complications are usually found as possible gonorrheal infection of the rectum, thus, it is not uncommon to have Bartholin or Skene's glands and ducts involved. These, in turn, will often subside spontaneously in the course of the routine treatment of the infected urethra, and it is better not to attempt any local treatment of these glands until expectant treatment has failed. It is in this stage that greater degrees of heat may help, and this may be given by the **medicated douche** up to 116° to 118° F (46.7° to 47.8° C) or with the Elliott machine, whereby the heat may be pushed up to 130° F (54.4° C).

3 With the *chronic stage* it is important to try to estimate what organisms are responsible for the continued symptoms. Occasionally symptoms continue because of a persistent virulent infection by the gonococcus. It is much more likely, however, that the gonococcus has passed out of the picture and that the symptoms are the result of infection with the streptococcus or actinomyces. If the chronic symptoms are due to the gonococcus, especially perimetritis, continued **heat therapy**, as **prolonged hot douching**, **Elliott machine treatment**, or **diathermy**, will undoubtedly be effective. If the streptococcus or actinomyces is the offender, probably little will be accomplished.

It is in this stage that complications are confronted that have not yielded to expectant treatment and it becomes necessary to consider radical measures.

Thus, *intractable Skene's glands* should be **irrigated with an antiseptic solution** through a small malleable tipped needle made for this purpose. If this is not efficacious, the gland should be obliterated by the passage of an electric cautery needle down through the duct.

*Periurethral abscess* should be treated expectantly by careful **massage**, the **abscess being emptied into the urethra** and the **sac filled with an irritant antiseptic solution**. These should be opened surgically only when this expectant method has failed.

If *Bartholin glands* do not subside with expectant treatment, careful **resection** should be done, preferably by the intravaginal route, as described elsewhere.

Persistent *lesions of the cervix* may call for radical treatment. If there are chronic sluggish erosions, it is important to know by culture what organisms are responsible. If, as is often the case, *actinomyces* is responsible, **iodine therapy** should be given by mouth and locally.

Careful **coagulation** or **cauterization by the electric needle** is often indicated, and in selected cases the **conization of the cervix** is valuable.

Operative intervention on tubes and ovaries infected by the gonococcus should be done only for urgent or definite reasons and should be avoided whenever possible. Spreading gonococcic peritonitis is rare but may be fulminating in character, especially in young girls, in whom it may simulate a ruptured appendix and calls for prompt operation. The perimetritic exudate of the acute and subacute stages may become completely absorbed. The sealed-off gonorrheal pyosalpinx soon becomes sterile pus and may subside, and the possible functional return for these damaged organs is not yet fully appreciated.

There is considerable division of opinion in regard to the efficacy of **vaccine therapy**. The author had on vaccine therapy 30 cases (3 billion upward); 5 cases on small doses (3 billion maximum), and on routine treatment 30 cases.

The vaccine was given intramuscularly in the deltoid region of the arm. The number of doses given varied from 5 to 21, with an average number of approximately 15. The initial dose was in most cases 3 billion organisms, and each consecutive dose was increased by half the preceding one, if reactions on the part of the patient were not unduly severe. The maximum dose given to any patient was 56 billion organisms. Most patients did not receive higher than 40 billion organisms, as they reacted severely before that point was reached. When reactions were very severe, the dosage was reduced and again increased carefully, or in some cases the vaccine was continued at that particular dose. The interval between each dose was 7 days.

Reactions, local and general, occurred in nearly all cases, the severity of which was in general in proportion to the dose, but they varied considerably in discomfort after an 8 billion dose, while others did not complain after 20 billion. As a rule, reactions were not severe until the 8 billion mark was passed. General reactions consisted of nausea, vomiting, chills, headache, malaise, elevation of temperature to from 99° to 103° F (37.2° to 39.4° C), and rapid pulse. A few patients complained of pain in the pelvic region. The patient returned to normal, as a rule, in from 24 to 48 hours.

Local reactions caused much discomfort and again, allowing for the individual susceptibility of the patient, were in proportion to the dose. They consisted of an area round the site of injection of marked swelling, redness and induration, acutely tender and painful, in other words, a local cellulitis. In some cases, after the larger doses, this area was from 4 to 6 inches in diameter and did not, as a rule, subside for 4 or 5 days. The gonococcus vaccine was prepared by the New York City Bureau of Laboratories.

Vaccine therapy is not a specific for the cure of gonorrhea. It is, however, probably a very valuable form of treatment in the acute and subacute stages of



the disease. This is probably true also in chronic cases in which the main offending organism is the gonococcus. It is probably not of value in cases due to "mixed" infection.

In the acute and subacute stages, vaccine therapy will probably shorten the period of hospitalization. However, the great drawback of severe reaction from this treatment, especially with large doses, is to be considered. It is questionable whether very large doses are justifiable, because of these reactions.

Probably vaccine therapy in smaller doses, combined with indicated routine treatment, would be a more desirable type of treatment.

Vaccine therapy is of sufficient importance to warrant further careful study into dosage, complement fixation reaction, and tests for proof of cure.

**ACUTE GONOCOCCIC PERITONITIS.**—Thomas Fitz-Hugh, Jr (J A M A 102.2094 (June 23) 1934) describes 3 cases of what is believed to be acute gonococcic peritonitis of the right upper quadrant in young women. The clinical and pathologic features are sufficiently distinct and uniform to justify the belief that the diagnosis may sometimes be made without great difficulty.

These cases, which represent the acute stage, help to complete the picture of the condition the end stage of which has been described by Curtis as "violin-string" adhesions between the anterior surface of the liver and the anterior abdominal wall occurring in women with present gonorrheal salpingitis or a previous history of that condition.

**Diagnosis.**—The clinicopathologic picture is described by the author as follows:

At some indefinite time, presumably following a previous gonorrheal infection, or possibly a reinfection, there occurs a brief period of leukorrhea, slight transient dysuria, cramps and perhaps a somewhat abnormal menstrual epoch. This train of symptoms suggests that a mild pelvic reactivation has occurred. Vague, low abdominal pain, distention and slight irregular fever follow promptly. Within from 1 to 3 weeks, sometimes after a brief interval of apparent quiescence, there occurs acute severe pain in the upper part of the abdomen, with distention and rigidity, which quickly localizes in the right upper quadrant. The pain in the right upper quadrant, rigidity and febrile relapse last for from a few days to a week and simulate very closely the picture of acute hydrops or acute empyema of the gall-bladder. The pain is made worse by coughing, sneezing, laughing or twisting the trunk muscles, and it is not relieved by strapping the lower part of the chest. A quiet deep breath does not cause much pain and the diaphragm moves fairly well. The peristaltic sounds are normal or only slightly diminished. The anterior abdominal wall below the right costal border is rigid and exquisitely sensitive. A crunching to and fro type of friction may readily be heard just over this area of the abdominal wall, at least during the subsiding stage of the acute process. The fever, pain, distention and rigidity subside within from 3 to 6 weeks from the first onset of symptoms. After this, the "chronic stage" begins, which may be symptomless or characterized by the later manifestations described by Curtis. The prognosis for recovery from the acute stage is uniformly good, and the ultimate outlook as to life itself is

apparently equally good. It would seem probable, however, that recurrent gonococcic invasions of the right upper quadrant might occur in certain cases.

During the stage of acute peritonitis in the upper part of the abdomen there is little or no leukocytosis and only a moderate "left shift" in the neutrophil formula. There is, however, a marked acceleration of sedimentation rate. The gonococcus may be obtained from the peritoneum during the (subsiding?) acute stage if the surgeon is fooled into operating. The gonococcus may or may not be obtained subsequently from the cervix or the urethra. A reasonable doubt as to the diagnosis must remain if the organism is not demonstrated. Sometimes in these cases there is apparently no gross evidence of residual gonorrhea in the pelvis. The gonococcus complement fixation test is not helpful (negative in 2 instances and positive in 1 during convalescence from the acute phase). It should be emphasized that these cases do not seem to fit the picture of the previously reported instances of virulent generalized acute gonococcic peritonitis, which is said to be very uncommon.

The clinical manifestations of this syndrome would seem to be rather clear cut. It is probably true that internists and general practitioners, who would be the most likely observers of the condition, have overlooked a number of these cases. It is obvious that the *differential diagnosis* of the condition must include a careful consideration of basal pleurisy, pneumonia, "intestinal grip," "devil's grip," colitis, cholecystitis, perforating peptic ulcer, pyelitis, an early stage of shingles, appendicitis and all forms of peritonitis. On the operating table the appearance of the lesions has a greater resemblance to a mild localized "zucker-guss" change, with little or no fluid, than it has to an acute peritonitis. It should not be necessary, except in unusual circumstances, to establish the diagnosis at operation.

**CERVICAL GONORRHEA.**—S. D. Breckinridge and A. J. Whitehouse (Am J Obst and Gynec 28:445 (Sept) 1934) discuss the treatment of cervical gonorrhea in the City Venereal Disease Clinic of Lexington, Ky. During a period of 2½ years approximately 10,000 visits were made by 574 patients. The routine followed in this clinic has been to make a thorough pelvic examination at the first visit, taking smears and a blood Wassermann and employing the dark-field examination where indicated. In patients with syphilis, the treatment of that disease is conducted in another section of the clinic. It is of interest to note, in passing, that, of the 574 patients seen, 273 had syphilis. In patients with positive smears, local treatment is initiated at the second visit, unless inflammatory masses are found. In the latter case, **foreign protein therapy** is instituted and from 5 to 10 doses are administered before local treatment is initiated. At first, various proprietary preparations were employed, but the present medication consists of sterile, fat-free milk. In the local treatment of the *cervix*, the **electric cautery** is employed. On account of its simplicity and the wide choice of tips, the Post instrument is used. In the parous cervix, which has not been extensively injured, the rod-shaped tip is placed in the canal, the current turned on and the appearance of a narrow, white rim of cooked tissue awaited. In nulliparous cervices, a smaller tip may be required. In extensively *injured and eroded cervices*, accompanying **linear cauterization** of the erosion will be

required. Treatment is repeated at intervals of 3 weeks, smears being taken preceding each treatment, starting with the third. In the earlier cases, where the smears were taken before each treatment, there was an occasional persistent negative after a single treatment. However, this was so rare as to be negligible. After the first negative, the patient is required to return every 2 weeks for follow-up smears. This course serves a dual purpose, *i. e.*, it gives an adequate follow-up and, as a public health measure, it permits supervision of the prostitute class for reinfection.

In the 162 cases carried to a persistent organism-free condition, the number of treatments required varied from an occasional single treatment to a small group of refractory cases requiring from 8 to 11 treatments. The average number of treatments for the entire group was 3.6. In addition to this larger number that is considered cured, there is a small group of 7 patients that shows either persistent, or occasional, positive cervical smears, in spite of thorough treatment.

There was a considerable incidence of moderate *stenosis of the cervix*. This was considered sufficient to indicate **dilatation** in 18 cases. The dilatation was performed with the Hanks dilators and was gradually carried to the size 16 instrument in 3 sittings, at weekly intervals.

The feeling is that the cautery may be used in pregnancy for the treatment of gonorrheal cervicitis without undue fear of abortion. It is felt that any undue method of treating gonorrhea of the cervix that will render and keep organism-free 162 out of 169 patients, drawn principally from the prostitute class, is worthy of both consideration and confidence.

**VAGINITIS IN CHILDREN.—Treatment.**—In the adult, the thick cornified epithelium of the vagina is resistant to the gonococci and, therefore, gonorrheal vaginitis, *per se*, is uncommon. In children, however, the gonococci flourish on the thin delicate mucous membrane and eventually penetrate into the subepithelial spaces. In this manner the disease becomes resistant to local treatment.

Lewis reasoned that if he could by means of the estrogenic preparation **theelin** change the vaginal epithelium in the immature human to that of the adult type, the gonococcic infection would be eliminated. He carried out this form of treatment on 8 children who were selected as showing typical cases of gonorrheal vaginitis. The patients received daily hypodermic injections of 50 rat units of theelin. The total amount of estrogenic preparation administered in each case varied, the average total quantity being 2100 rat units. The average duration of the treatment was 21 days, the longest course continued for 98 days. He demonstrated by means of biopsy the remarkable changes that were effected by the estrogenic preparation. The results were exactly similar to those which Allen had obtained in the immature monkey. In his opinion, theelin, by inducing a proliferation of the vaginal epithelium, rapidly clears up the discharge and appears to eradicate the gonococci.

J. Huberman and H. H. Israeloff (J. A. M. A. 103:18 (July 7) 1934) used **amniotin** instead of theelin. One hundred rat units of hypodermic amniotin was administered 3 times a week on 5 patients of the series, while 1 child, aged

3½ years, received daily from 120 to 200 rat units of oral amniotin. At no time were there any local or constitutional reactions manifested as a result of the treatment.

It was noted that in the 3 chronic cases the vaginal discharge disappeared after 4 weeks of treatment. The children of this group were clinically cured after receiving a total average of 21 injections or 2100 rat units of amniotin.

The authors are of the opinion that the success of this mode of treatment depends mainly on the development of a layer of cornified epithelial cells. This layer of cells is analogous to the desquamating type of cells found in the normal adult vagina. The acquired layer of cornified epithelial cells acts as a protective barrier against the rapidly multiplying gonococci and thus prevents reinfections. On the other hand, the gonococci that have previously penetrated into the sub-epithelial spaces are destroyed by the normal phagocytic action of the leukocytic elements.

**GRANULOMA INGUINALE AND LYMPHOGRANULOMA INGUINALE.**—*Differential Diagnosis.*—In a discussion of the differential diagnosis of these two conditions (Queries and Minor Notes, J. A. M. A. 102: 560 (Feb. 17) 1934) it is pointed out that granuloma inguinale and lymphogranuloma inguinale have but 2 points of resemblance. They are both classed as venereal diseases and, unfortunately, they have names that are so much alike that they are confusing. Otherwise, the diseases are totally dissimilar.

Lymphogranuloma inguinale is due to a filtrable virus that can be transferred to several of the lower animals by way of subdural injections, causing an encephalitis. The incubation period of lymphogranuloma inguinale is from 1 to 2 or 3 weeks. The exact incubation period for granuloma inguinale is not exactly known, but probably varies from a few weeks to a month.

With lymphogranuloma inguinale there may be a primary lesion of the type of a papule, of a pustule, of herpetic process, or of a specific urethritis, which may be confused with gonorrhea. Following this primary lesion, which is usually evanescent in character, there is an involvement of the draining lymph nodes. The adenitis of lymphogranuloma inguinale is characteristic. The nodes in a chain become fused together in a large mass, which may reach half the size of a fist, and then the process breaks down, with multiple fistulous openings. Along with the local adenitis there may be systemic symptoms of malaise, loss of appetite, loss of weight, rheumatic symptoms, eruptions on the skin, and a temperature elevation which may be of the intermittent, remittent or continuous type. Occasionally, the elevation of temperature will persist over a long period, successive flare-ups accompanying the involvement of fresh lymph nodes.

In the female affected with lymphogranuloma inguinale the picture may be somewhat different, owing to the fact that most of the lymph channels running from the vulva drain into the nodes around the lower part of the rectum, resulting in an inflammatory reaction of these nodes and a secondary involvement of the rectal wall. It has been found that certain of these female cases, as a result of the local process, later present an inflammatory stricture of the lower rectal walls, which may be annular or tubular in character. Rarely, in a female, along with a stricture of the lower rectum, there may be excrescences developed round

the anal orifice, sometimes accompanied with fistulas, and there may also be more or less elephantiasis of the vulva and fistula formation going under the term "esthiomene."

Clinically, there should be no difficulty in making a differential diagnosis between granuloma inguinale and lymphogranuloma inguinale. Lymphogranuloma inguinale is essentially a disease of the lymph channels and of the lymph nodes, while granuloma inguinale is a disease affecting the skin itself; there is never an involvement of the lymph nodes in granuloma inguinale. In the latter disease there will be found a beefy red, generally somewhat raised, rather rugose, moist proliferation of the tissues, which is most characteristic in appearance. Instead of spreading by the lymph nodes, the disease spreads by contiguity and may spread by contact from the genitalia to the inside of the thighs. Or the process may spread from the genitalia down over the perineum and perhaps up into both groins by way of the skin. At no time, however, will there be an involvement of the nodes themselves. As a rule, there are no systemic symptoms in connection with granuloma inguinale. The diagnosis of granuloma inguinale may be greatly facilitated through making a smear from the local inflammatory tissue or removing a specimen of the tissue and making a smear on a glass slide with the undersurface of this tissue, as would be used in making a blood smear. The slide is then stained with either Giemsa's or Wright's stain, and specific Donovan inclusion bodies will be found, though probably with some difficulty, unless the physician is accustomed to the microscopic picture. Assistance may be obtained in making a diagnosis of lymphogranuloma inguinale by the so-called Frei test. This is a specific intradermal test performed in the same manner as a tuberculin test. The antigen consists of some of the sterilized pus taken from a bubo just before it is going to break down. Naturally, a test could not be made with pus taken from the patient who is to be tested. One-tenth c.c. of this material is injected intradermally, and in 48 hours there will be a raised, erythematous tubercle, from 0.5 to 1 cm. in diameter, in a positive case.

**Prognosis.**—The prognosis and outlook in either of these diseases is somewhat guarded, owing to the fact that in granuloma inguinale there is such a frequent tendency to recurrence and that in lymphogranuloma inguinale one of the serious complications, such as stricture of the rectum, may result before the disease is finally cured. It is true, however, that once lymphogranuloma inguinale is cured, the patient ordinarily has no further difficulty, and it is a question whether he is not immune for the rest of his life.

**Treatment.**—Strangely enough, antimony seems to be the best preparation for treatment of either of these diseases. In the past this has been used in the form of **antimony** and **potassium tartrate**, a 1 per cent solution being employed and an injection given intravenously of 3 c.c. ( $\frac{3}{4}$  dram) plus 7 c.c. ( $1\frac{1}{4}$  drams) of **saline solution**. The antimony and potassium tartrate is stepped up 1 c.c. (16 minims) at a dose, the injections being given once in 3 or 4 days until a maximum dose of 10 c.c. ( $2\frac{1}{2}$  drams) of the 1 per cent solution is given, and this may be continued for 10 to 15 or more injections, the kidneys being watched for evidence of irritation. Recently a new antimony preparation, **fuadin**, has come on the market (J. A. M. A. 100 1685 (May 27) 1933).

Fuadin is much easier to administer, since it may be given intramuscularly and with little discomfort to the patient. The injections are given once in 2 or 3 days, starting with a dose of 2 c c ( $\frac{1}{2}$  dram) and working up to a maximum dose of 5 c c ( $1\frac{1}{4}$  drams), a total of from 45 to 50 c c. ( $1\frac{1}{2}$  to  $1\frac{2}{3}$  ounces) of the preparation being given, which constitutes a course, which may be repeated within a month, if found necessary. With a case of lymphogranuloma inguinale, **rest in bed** is quite essential, and it may be necessary that some **minor surgical procedure**, such as opening necrosing lymph nodes, or even partial removal of a broken down lymph node, may be necessary.

**LEUKORRHEA.**—*Treatment.*—The difficulties of treating vaginal discharge are described by H. Breithreuz (Munchen. med. Wchnschr (July 6) 1934). Normally, the vagina contains Doderlein's lactic acid bacilli. Lavages, therefore, with lactic acid were believed to be beneficial. They, however, only have a temporary effect. The introduction of lactic acid bacilli has not proved successful. The last possibility is to ameliorate the conditions for the existence of the lactic acid bacilli. This is obtained by the sugar-treatment of the discharge, as the fact is well known that the glycogen, which is deposited in the epithelial cells of the vagina, acts as food for the lactic acid bacilli. Recently, **dextrovagin** has been introduced. It is a monosaccharide, pressed into the shape of rods, these rods being moistened with water before use and introduced deeply into the vagina. The patients may treat themselves at home. The treatment should be continued for at least 2 weeks. After menstruation, the rods should be introduced for some days. The treatment is not successful in cases of cervical infection, in gonorrhea, or in trichomonas infection. Exact bacteriological examination of the secretion of the vagina is essential. The author has treated 160 cases successfully. In unsuccessful cases disturbances of internal secretion may play a part.

**MATERNAL MORTALITY.**—The following items of interest have been abstracted from the survey on "Maternal Mortality in Philadelphia, 1931—1933, Report of Committee on Maternal Welfare, Philip F. Williams, Chairman," as presented to the Philadelphia County Medical Society on May 23, 1934.

1 **Births.**—The number of births in Philadelphia has dropped in the last 10 years from 41,343 in 1924 to 29,569 in 1933 but there has been no appreciable reduction in the maternal death rate. From a study of the practically stationary maternal mortality rate, it is obvious that the advantages of modern surgical technic and increased hospital facilities for specialized obstetrical practice have brought no definite decrease in the number of maternal deaths. In the past decade the maternal mortality rate has dropped only from 8 per 1000 live births in 1921, to 6.6 in 1932, although the birth rate fell from 23.8 per 1000 population to 16.22.

2 **Maternal Death Rate.**—The maternal death rate as calculated by this survey showed 717 deaths to 99,579 total births or 7.09 deaths per 1000 total births. Of these 647 occurred at hospitals and 70 at home. Eliminating the 78 nonobstetrical causes of death and calculating the rate on live births alone, it was 6.39 per 1000 live births.

The principal causes of death and their percentage distribution was as follows ·

Septic abortion .....	162 patients or 22.6 per cent.
Septicemia .. . . .	119 patients or 16.6 per cent.
Albuminuria and eclampsia .....	85 patients or 11.9 per cent.
Accidents of labor.. .. .	79 patients or 11.0 per cent.
Hemorrhage .. . . .	62 patients or 8.7 per cent
Embolus and sudden death.....	44 patients or 6.1 per cent
Extrauterine pregnancy ... ..	33 patients or 4.6 per cent.
Abortion, nonseptic .. .. .	26 patients or 3.6 per cent
Pernicious vomiting . . . . .	24 patients or 3.3 per cent.
Accidents of puerperium.... .	5 patients or 0.7 per cent
Nonobstetrical causes .....	78 patients or 10.9 per cent

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Total deaths . . . . . 717 patients

3 *Preventability Due to Physician.*—If a patient died from a long complicated labor through failure to recognize, by means of pelvimetry, the presence of pelvic deformity, the physician was considered responsible for that death.

The physician should make a vaginal examination in the early months in order to diagnose, if possible, the presence of abnormal pregnancy (ectopic). In cases where he failed to do this and the patient died of hemorrhage or shock, the responsibility for the death was assigned to the physician.

The physician should be able to recognize the presence of disproportion between the fetus and the pelvis. He should know if there is a malposition or malpresentation before the onset of labor. It is essential that he inquire into the past maternal history very carefully so as to learn if there were any complications in the previous deliveries. It is in his province, too, to impress upon the patient the need for early and regular examinations in order to recognize as soon as possible any signs, symptoms or abnormalities, such as early toxemia.

The physician was considered responsible for deaths in another group of cases, namely, where the abnormality was recognized but the treatment was inadequate. For instance, if the physician failed to have consultation, either through the clinics or by other individual physicians, for patients whose general condition warranted more careful study, especially in renal, cardiac or pulmonary complications, he was held responsible for the deaths. He was considered at fault when he failed to have the patient hospitalized promptly for serious complications that could not be treated adequately at home, such as cases of placenta previa, eclampsia or disproportion.

The physician was thought responsible if he failed to recognize that long labor and loss of blood tend to lower tissue vitality and as a consequence increase the possibility of infection.

He was considered responsible for death if he delayed in emptying the uterus in cases of placenta previa or premature separation of the placenta, or if he delayed in operating on cases of ectopic gestation with evident severe hemorrhage, unless transfusion was needed and was available immediately. If he failed to pack the uterus following delivery in cases complicated by placenta previa, premature separation of the placenta, or inverted uterus, he was thought to be responsible.

In cases where death was considered due to anesthesia, the physician was thought to be at fault. Such cases included deaths from spinal anesthesia, or from experimentation with new drugs such as anesthetics, as well as cases in which the anesthetic was administered by an untrained person.

4 **Illegitimacy.**—The Analysis Committee placed the responsibility on the patient in 51 of the 79 deaths in illegitimate pregnancies. (Four per cent. of the total births included in this survey were illegitimate.) The avoidable feature was ignorance of the consequences of induced abortion in 39 cases, failure to obtain prenatal care in 4, and disregard of symptoms in 8.

5. **Prenatal Care.**—This was adequate in 216 cases, inadequate in 193 cases, none in 297, unknown in 11.

6. **Septic Abortion.**—One of the outstanding facts discovered is that 22.5 per cent. of the total deaths studied were caused by septic abortion (under 28 weeks). One hundred and two of these 162 deaths followed illegal induction. The laity has not been educated sufficiently to realize the dire consequences of illegally induced abortion. Nor is the seriousness of the criminal act recognized. This is shown by the fact that, during the 3 years of the survey, no conviction was obtained for this crime in Philadelphia. If this group of 102 cases could have been eliminated, the deaths would have been reduced 14 per cent. The death rate from sepsis was far greater in the cases under 28 weeks pregnancy than in those over 28 weeks.

Of the 162 deaths following septic abortion, 114 were in married women and 48 were in illegitimate pregnancies. This ratio of almost 3 to 1 indicates clearly that the cause of self-induced or criminal abortion is not, as has been commonly believed, the result of illegitimate pregnancies, but, in far greater measure, is a direct corollary of economic and social conditions.

The Committee feels that a dictum should be laid down in regard to treatment of these cases. In septic or potentially infected abortions, the uterus should not be invaded further than to remove material from the cervix for better drainage of the uterine cavity or for the control of hemorrhage.

7 **Abortion With No Mention of Sepsis.**—There were 26 deaths, 3.6 per cent. under 28 weeks pregnancy, due to abortion not associated with sepsis.

The outstanding feature of this section is the predominance of hemorrhage as a cause of death. Early recognition and prompt treatment of this condition should be borne in mind.

8 **Therapeutic Abortion.**—There were 16 deaths following abortion performed for therapeutic reasons.

9. **Ectopic Gestation.**—Thirty-three women died from this cause. Failure in diagnosing this condition due to ignorance of the significance of symptoms is deplorable. That one-fifth of the cases were not operated upon reflects upon both physician and patient. This could be eliminated in part by early examination of women with amenorrhea during the reproductive period. That gratuitous surgery added to the burden is shown in the finding that almost half the cases discussed here had had coincident operative manipulations other than the removal of the affected tube. It was noteworthy that one-fourth of this group of deaths was caused by *septic infection* after operation.



10 *Puerperal Hemorrhage*.—These totalled 77 deaths divided as follows: placenta previa 25, premature separation 19, postpartum hemorrhage 33.

11. *Placenta Previa*.—During the period of the survey the hospitals of the city reported a total of 342 cases of placenta previa with 25 deaths or 7.31 per cent. Frequently the diagnosis of placenta previa was not made until a serious or, at times, a fatal hemorrhage had occurred. The improper management of such a case, however, presented a much more serious problem than the failure in diagnosis.

The choice of means to control the hemorrhage was often questionable. The application of the method of delivery was unskillful and the lack of asepsis was shown in the proportion of septic infections incurred. Induction of labor in placenta previa is a debatable question. Failure to properly pack the uterus after delivery in these cases and the omission of transfusions shows evidence of lack of preparedness for emergencies. When placenta previa is diagnosed, a method of delivery for the particular case should be selected and properly performed and the necessary adjuvant measures should be carried out promptly.

12 *Premature Separation of Placenta*.—Nineteen women died of this cause. All showed preliminary symptoms so that there was sufficient time for more prompt treatment. The error in judgment on the physician's part was often poorly selected time of operation. All cases of premature separation delivered by the vaginal route should be packed immediately after delivery, and blood volume should be restored by blood transfusions or by the intravenous injection of other fluids.

13 *Postpartum Hemorrhage*.—There were 33 deaths in which postpartum hemorrhage was the primary cause of death in 27 and the contributory cause in 6. In 24 of these cases labor had continued for more than 24 hours. The relation of labor to noncontractility of the uterus seems to have been overlooked. The technique of packing the uterus must be questioned when it is shown that 19 of these cases died in spite of uterine tamponade. An outstanding suggestion is that vaginal packing be discarded for full intrauterine packing. That but one case received a blood transfusion is a shocking admission of lack of preparedness for such emergencies, provided it was not due to error in judgment in the handling of the case. The relation of manual removal of the placenta to postpartum hemorrhage was high, and the need for the operation was not explained sufficiently in the records. It appears incredible that a woman should bleed to death from a torn cervix with no attempt at repair.

14 *Puerperal Septicemia*.—One hundred and nineteen women died from puerperal sepsis exclusive of septic abortion or septic infection following ectopic gestation.

Ninety-eight of the deaths followed hospital deliveries and 21 followed home deliveries. Twelve of the home cases were referred to the hospital later. These 98 deaths represent 30.6 per cent of the 320 deaths following hospital delivery in women over 28 weeks pregnant. In 77 of these cases sepsis developed in the hospital. In 21 the infection occurred at home before admission, although delivery occurred in the hospital. The incidence of hospital delivery sepsis is 1.17 per 1000 live births and of home delivery sepsis is 1.44 per 1000 live births.

The Analysis Committee decided, in regard to preventability, that 99 or 83 per cent of these 119 septic deaths could have been avoided. This fact is regarded as one of the most outstanding developed from this survey. To the physician was ascribed the responsibility in 97 cases; to the patient in 2; 20 deaths were regarded as nonpreventable.

15 *Albuminuria and Eclampsia*.—The third largest cause of death in this survey was albuminuria and eclampsia, responsible for 85 deaths. As half of these women received at least the minimum amount of supervision necessary for adequate prenatal care, there must be some skepticism as to the exact quality of such care. Every pregnant woman should be regarded as a potential eclamptic. More thorough study in early pregnancy is necessary to determine possible functional inabilities. Earlier hospitalization is essential for mild degrees of toxemia. Prompt termination of pregnancy is imperative in toxic cases failing to respond to treatment. Emergency surgery showed to no advantage in the treatment. Of the 57 per cent of cases regarded as preventable, the patient was considered responsible in 61 per cent.

16 *Vomiting of Pregnancy*.—This caused 30 deaths. The majority of these cases of pernicious vomiting occurred in primiparous women, who failed to seek medical assistance early. Sixty-six per cent. of the hospitalized patients were in only fair condition on admission. The number of deaths occurring after therapeutic abortion would seem to show that the operation had been postponed beyond a reasonable time for expectancy of recovery. There was a high incidence of other puerperal complications or other intercurrent diseases to further lower the resistance of these women.

17 *Embolus and Sudden Death*.—Forty-four deaths were certified to have occurred from phlegmasia alba dolens, embolus, or sudden death. There is little doubt that a considerable number of deaths are attributed to pulmonary embolism which should really be relegated to trauma or shock or both. The diagnosis of embolus is a simple explanation and salves the conscience of the person in attendance.

18 *Operative Deliveries*.—The most striking change in obstetric practice in the past decade and a half has been the great increase in operative deliveries. A certain few have raised their voice on every occasion against the tide of radicalism, but apparently without stemming the rise.

It was difficult for the Analysis Committee in reviewing the answers to the hospital questionnaire received each year, to believe that 18 Cesarean sections were even relatively indicated in a one-year delivery service of 142 births.

There were 68,733 hospital deliveries in the 3 years. There were 19,237 operative deliveries and 49,496 spontaneous deliveries. The total operative incidence was 27.9 per cent. There were 1775 Cesarean sections in hospitals, an incidence of 2.58 per cent.

There were 14,292 forceps deliveries or 20.7 per cent. There were 112 deaths associated with either attempted or successful forceps deliveries. There were 1050 versions performed in the hospitals during the survey, no information was available as to the number in this group which were elective. There was an

incidence of 1.52 per cent versions performed in 68,733 hospital deliveries. Sixty-five deaths followed these versions.

There were 18 craniotomies performed in the 68,733 hospital deliveries. There were 2039 breech extractions or breech decomposition and extractions performed among the 68,733 hospital deliveries—an incidence of 2.96 per cent.

19. **Cesarean Section.**—In 1775 Cesarean sections there were 98 deaths following, 64 considered as preventable and 34 as unavoidable.

Postmortem sections were performed 12 times and in 2 the child was born alive.

20. **Breech Extractions.**—There was reported a total of 2039 breech extractions or decompositions and extractions which were performed in the hospitals. This group represents an incidence of 2.9 per cent of the 68,733 hospital deliveries. There were 37 deaths associated with breech presentations, 5.1 per cent. of the 717 cases studied.

21. **Removal of Placenta.**—The placenta was removed manually 43 times or 15 per cent of the 286 women over 28 weeks pregnant. This procedure was used after 35 operative and 8 spontaneous deliveries. Of great interest was the group of 8 deaths where the delivery was spontaneous and the placenta removed manually. All but one of these women were multiparas, all but 2 were over 30 years of age. The indication for the removal or extraction in 6 of these cases was adherent placenta, in 1 retained placenta, and in the remaining case no indication was given. The time interval for removal of placenta after birth varied greatly. In 4 it was less than an hour, in 2 the interval was 3 hours, and one 7 hours, and in the last case, 10 hours.

22. **Nonobstetrical Causes of Death.**—Seventy-eight or 10.9 per cent of the series of 717 deaths fell in this group. The largest single cause was pneumonia, which included 23 cases.

There were 16 deaths from cardiac disease and in 53 other patients who died it was a secondary cause. Thus about 1 per cent of all pregnancies are complicated by heart disease and about 6 per cent. of these die.

Every cardiac patient should receive careful supervision during pregnancy in order to assure the best possible health at the time of labor and puerperium. This necessitates a careful physical examination, repeated attempts at evaluation of cardiac reserve and close cooperation between obstetrician and cardiologist. A pregnant patient who goes into heart failure is a victim of neglect. "Every pregnant patient who, upon examination, gives (1) a positive etiologic history, such as acute rheumatic fever or chorea, (2) symptoms of heart disease, such as dyspnea, palpitation, edema, night starts, sighing, nose-bleeds, or (3) signs of heart disease, such as tachycardia, enlargement of the heart, venous pulsation, murmurs, whether basal or apical, systolic or diastolic, gallop rhythm or third sounds, should be referred to a cardiologist for complete diagnosis and recommendation for definite treatment.

23. **Deaths in Undelivered Women.**—There were 91 women in this series of 717 who died undelivered or unoperated upon.

24. **Stillbirths.**—During the period of this survey 4185 stillbirths were registered in a total of 99,579 births in Philadelphia, making a stillbirth rate of

42 per 1000 total births. The death rate among women who had stillbirths, 230 to 4185, was 55 per 1000 births, as contrasted with a general maternal mortality rate during the survey of 7 per 1000 births—almost 8 times as great. In the 84,470 white births there were 3198 stillbirths, a rate of 37.8 per 1000. In the 15,109 negro births there were 987 stillbirths, a rate of 65.3 per 1000. The ratio of negro to white stillbirth rate was as 1.7 to 1. In the 3885 illegitimate births there were 234 stillbirths, a rate of 60 per 1000. In the 95,694 legitimate pregnancies there were 3951 stillbirths, a rate of 41.2 per 1000. The ratio between illegitimate and legitimate was as 1.5 to 1.

**25. *Recommendations Made by the Committee on Investigation of Maternal Mortality:***

After careful consideration of the facts revealed by the survey, the Analysis Committee felt that the problem presented 4 phases:

- 1st—Self-induced and criminal abortion;
- 2nd—Errors in judgment on the part of the medical profession;
- 3rd—Lack of appreciation of the need of prenatal care by the laity;
- 4th—Failure of hospitals, organized medicine and allied agencies to grasp fully their responsibilities and opportunities

It is impossible to face the abortion situation frankly as has been done in some foreign countries, due to existing laws in relation to the giving of contraceptive advice. Meanwhile, it is the responsibility of the medical profession and interested lay groups to inform the public of the perils of nontherapeutic abortion.

Errors in judgment may be summarized as being caused by inexperience, failure to note important danger signals, undue faith in operative interference, and a willingness to "take a chance." To remedy these conditions, there must be reorganization in the training of obstetrics, closer supervision of internes, and graduate instruction for physicians.

Education of the laity is the responsibility of the physician. Every expectant mother should be taught the danger, not only to herself but also to her baby, resulting from improper supervision in toxemias. A well-conducted campaign would aid greatly in eliminating "ignorance of the patient" as a factor in maternal deaths in these cases.

Hospitals, medical societies and allied agencies should assume more responsibility regarding the factors which tend to reduce maternal mortality. Such organizations have wide influence both with the medical profession and with the lay public, and they should embrace every opportunity to advance the practice of obstetrics through cooperative education and legislation.

If the maternal death rate in Philadelphia is to be reduced, certain changes must be made in the attitude and procedure of various groups involved. To this end, specific recommendations are made.

As the responsibility rests primarily with the profession, physicians must assume leadership in the double rôle of raising the educational standards of doctors, nurses and midwives, and of informing the laity of the need of adequate maternity care.

**PHYSICIANS.**—Education of the medical profession constitutes an equally important part of this general program to reduce maternal mortality. More op-

portunities should be offered to the physician desirous of advancing himself in the art and science of obstetrics. In some of the larger general hospitals, the material seems sufficient to warrant a residency in obstetrics for the education of the young specialist without seriously interfering with the training of internes.

There is a dearth of seminars and demonstrations in obstetrics open to the general practitioner. If such courses were arranged regularly and advertised sufficiently, they might well serve as stimulants for the general practitioner.

**INTERNES.**—In certain institutions, internes are allowed wide latitude in operative obstetrics without supervision. This is injudicious and prejudicial to the best interests of the patient. In the limited and constantly diminishing clinical material in this branch of medicine, opportunity should be sought to instruct internes and residents in the contraindications as well as the indications for operations in obstetrics, also in the selection and administration of anesthetics. Further, for the protection of the patient, a regulatory limitation of any interference by the interne is essential.

This survey showed that a large number of unsupervised deliveries are conducted by students in the out-patient departments of teaching institutions. From an educational standpoint, absence of supervision of students would appear as inexcusable in obstetrical practice as in surgical procedures.

It is apparent that there is need for greater concentration on the elementary principles of obstetrics, and the teaching of conservative labor, on proper antenatal hygiene, and on the essentials of postpartum care.

**NURSES.**—The teaching of nurses should ground them in the elements of practical obstetrics. They should be able to recognize abnormal symptoms and should obtain, when necessary, earlier hospitalization in potentially dangerous conditions. As in the case of physicians, facilities should be provided for the further education of the nurse who wishes to specialize in obstetrics.

**MIDWIVES.**—This survey has shown that the midwife is an almost negligible factor in mortality in Philadelphia. Should the present standard be maintained, and should the progressive decline in midwife practice continue, she cannot be regarded as of importance in this problem.

It is recommended, however, that some provision be made to supply prenatal care for women registering with midwives. Arrangements might be made through the nursing system of the Division of Child Hygiene whereby every midwife case could obtain at least a physical and pelvic examination.

**LAITY.**—The number of seemingly preventable deaths attributed to the patient is entirely too high. It seems that ignorance and lack of cooperation could be ruled out as avoidable factors through proper education.

Physicians should instruct the public as to the dangers of induced abortion. This is essential if any progress is to be made in combating this increasing and prevalent socio-medical problem. Septic abortions—whether self induced, criminal, or spontaneous, are the largest single puerperal cause of death in this city. The largest proportion of these deaths is among married women, many of whom have living children. This would seem to indicate that under present economic conditions, the difficulty of providing for children and the desire to give them better opportunities may be the fundamental cause. A number of foreign countries

have faced the problem by allowing the free giving of contraceptive information, or by legalizing abortion. The Committee is not in agreement as to the advisability of changing the law in regard to either of these procedures.

Physicians should also stress the relation of proper antenatal supervision to preventable catastrophes. The nature and importance of danger signals in pregnancy must be explained to the prospective mother and her cooperation insisted upon.

As surgical asepsis at delivery constitutes a part of adequate maternity care, women should be taught the need for the eradication of foci of infection in the cervicovaginal tract, the avoidance of intercourse in late pregnancy, and the necessity for scrupulous personal hygiene. It is important also to explain the changes that occur in the pelvic organs during convalescence and to stress the value of follow-up examinations as the final step in complete obstetrical supervision.

There is need, too, to teach the laity that maternity care should be remunerated sufficiently to encourage the physician to give his best professional efforts to his patient. The public should realize that the laborer is worthy of his hire.

**ORGANIZED MEDICINE.**—Organized medicine must play an important part, too, in the reduction of the maternal death rate. A comprehensive program has been arranged in this connection, but it seems unnecessary to present it at this time. The details will appear in the printed report of this survey.

**HOSPITALS.**—Hospitals are intimately associated with maternal mortality as it is, of necessity, in such institutions that the largest number of births and maternal deaths occur. It is the duty of the hospital staff to investigate fully and frankly all the circumstances relating to maternal deaths in order to prevent repetition of avoidable errors.

It is essential that every hospital provide means for isolation and segregation of potentially infected cases. An allowance of antenatal beds is needed to provide proper care for cases requiring observation and treatment.

There should be an adequate staff of trained social workers in every prenatal clinic to provide complete follow-up of abnormal cases.

**CONCLUSIONS.**—The solution of this question of reducing maternal mortality in Philadelphia is education. This should begin in the medical schools by changing the curriculum in regard to the teaching of obstetrics. It should extend to the entire medical profession, in order to make doctors realize the danger of ignoring symptoms requiring hospitalization or consultation. Physicians can acquire good judgment as to the management of obstetrical cases only through adequate training and experience. Instruction of the laity as to the meaning of adequate maternity care is also of importance. Such teaching, however, must be undertaken by the medical profession and not left to the nonmedical articles of very doubtful value that appear in lay journals and magazines. Education is the keynote of the situation and the responsibility belongs to the medical profession.

**MONSTROSITIES.**—G. W. Gustafson (*Surg. Gynec. Obst.* 59:223 (Aug.) 1934) notes that there are only 2 means of absolute diagnosis of intra-uterine monstrosities available, *i. e.* (1) employment of the x-rays, and (2)

direct palpation of the abnormal condition vaginally. Only within the past 10 years has roentgenology been so perfected as to be of assistance in this diagnosis. As it is needless expense to the patient to use the x-ray in every case of pregnancy, it is imperative to select those cases for study that show clinical signs or associations pointing to the presence of a monstrosity.

During the past 3 years the author has encountered 5 cases of monstrosities in all of whom a diagnosis was made before delivery. In 4 of the cases this was made by the x-ray but in each case there was a definite indication for roentgenology either to confirm the tentative diagnosis or to assist in the diagnosis of intrauterine death. The fifth case was one of teratocormus cyllosoma. Convulsive movements of the fetus and irregular fetal heart tones were not observed in any of the cases. Of the 5 mothers, 3 had previously borne healthy babes and in no case was syphilis a likely factor.

The first case was examined by x-ray because of the presence of acute polyhydramnios. The second case was discovered while attempting to find x-ray evidence of fetal death. The third case was submitted to the x-ray because of the abnormally large fetal head, while the fourth was found because of careful frequent abdominal examinations revealing the absence of a demonstrable head either in the pelvis or in the fundus.

The intrauterine diagnosis of fetal monstrosity is to be highly desired. Cases of suspected intrauterine death should be x-rayed. In addition to the cardinal findings of fetal death—overlapping of bones of the skull, acute angulation of the spine, and compression of the thoracic cage—often the presence of a monstrosity will be shown.

During the latter months of pregnancy, repeated abdominal examinations are urged. Failure to outline a normal fetal head abdominally or in the pelvis is a definite indication for x-ray examination, as is every case of marked polyhydramnios. When possible, every candidate for Cesarean section should be x-rayed, especially so in cases of placenta previa.

**OVARY.—CARCINOMA.**—In discussing 5-year results in the treatment of 24 cases of cancer of the ovary, B. M. Anspach (*Surg. Gynec. Obst.* 58: 448 (Feb. 15) 1934) reports that there are 7 cases now living and apparently well at the end of 5 or more years, a curability of 29.1 per cent; in 5 of the 7 cases, 17.24 per cent, there is no evidence on palpation of any pelvic disease. In 2 there are small masses or areas of pelvic induration without any abdominal or pelvic symptoms. The patient apparently is cured, but fibrotic tissue has been left behind.

Clinically, ovarian cancers are classified as follows:

- I. The disease is limited entirely to the ovary and completely removable.
- II. The disease is mostly limited to the ovary but there is some spread that is removable with the ovary.
- III. The disease is not limited to the ovary and there are spreads that are only partly removed.
- IV. The disease is widespread and completely inoperable.

In Class I—1 living 11 years, 2 dead, 1 untraceable, 1 living 4 years, and 1 living nearly 2 years.

In Class II—4 living more than 6 years.

In Class III—2 living, one 7 years and one 11 years.

In Class IV—All dead within 1 year.

**GRANULOSA CELL CARCINOMA.**—A cause of postmenopausal hemorrhage not generally recognized by surgeons and pathologists, *viz.*, granulosa cell carcinoma of the ovary, is discussed by E. Novak (Am. J. Surg. 24: 595 (June) 1934). While rather rare, this tumor is of great biological interest, particularly because the tumor cells produce folliculin, and thereby, in the postmenopausal patient, bring about a species of rejuvenation in the uterus. Menstruation, or at any rate a periodic bleeding, is reestablished, and the uterus often is as large as, or larger than, its premenopausal size. Hyperplasia of the endometrium, a condition commonly observed only during the reproductive years, is noted in these patients. When well-marked hyperplasia of the endometrium is revealed by diagnostic curettage in cases of bleeding in elderly women, there should be strong suspicion of granulosa-cell ovarian tumor, even though none can be felt, and laparotomy would seem justified. If a tumor can be palpated, the suspicion becomes almost a certainty.

Three additional cases of this type are reported, including one in which the tumor was of very small size, so that it caused no ovarian enlargement. This tumor proved to be of especial interest, not only because of its unusual histological structure, but because of the pathologic physiological effects which it produced upon the endometrium. The possibility of lutein-like transformation of the granulosa cells of the tumor is discussed as a possible explanation of the secretory changes seen in some of the endometrial glands. The significance of granulosa-cell tumors is discussed also from the standpoint of other physiological problems, such as the cause of menstrual bleeding, and the possibility of menstruation without ovulation.

E. Novak and J. N. Brawner (Am. J. Obst. and Gynec. 28: 637 (Nov.) 1934), describe a clinical and pathologic study of 36 cases. There is now quite general acceptance of Meyer's view that granulosa cell tumors arise from granulosa cell "rests" (granulosa-ballen), left over from the early oophorogenetic phase of ovarian development. In this series 5 occurred in children before puberty, and in all there were manifestations of precocious puberty and, with one exception, menstruation. In only 6 of their group were the patients definitely beyond the menopause, although in 10 others the patients were in the fifth decade. The effects of these tumors upon the menstrual function are what would be expected from the production of excessive amounts of folliculin. Tumors before puberty produce precocious menstruation; those during reproductive life bring about disturbances quite analogous to those so characteristic of hyperplasia of the endometrium (menstrual excess with amenorrhea at times), while tumors after the menopause tend to reestablish a menstrual or pseudomenstrual type of bleeding.

Aside from the effects upon menstruation, there has been noted, in a certain number of reported cases, a stimulating effect upon the structure and function of



the breasts. In all the cases in children there was marked mammary overgrowth, though no secretion was present. In older patients, similar hypertrophy, with a secretion of a colostrum-like fluid, was noted in some instances.

The special biologic effects of these tumors are due to the fact that they secrete folliculin and, in some cases, also progesterin. The folliculin effect has been amply demonstrated by the production of estrus in castrated mice following the injection of extracts of the tumor.

The degree of malignancy of granulosa cell carcinoma is much less than that of ovarian cancer in general, and the evidence certainly supports this view.

In spite of this, at least 9 of the patients showed unmistakable evidence of malignancy, either in the picture presented at operation (6 cases) or in the development of recurrences (3 cases), sometimes surprisingly soon after operation.

**Diagnosis**—As a rule, the tumor may be readily demonstrated by bimanual or abdominal examination, and, for that matter, has often been noted by the patient herself. In women during the reproductive epoch, the granulosal nature of the neoplasm is usually not suspected until operation, and perhaps not even then. When there is any clinical suspicion of the character of the tumor, quantitative studies of the hormone content of the urine may prove of value.

It is in childhood and in the postmenopausal years that the preoperative diagnosis of the nature of the tumor can most often be made at least presumptively. This is because of the physiologic and biologic effects produced by the growth, which stand out sharply in the patients at these ages.

If an ovarian tumor is demonstrable in a child with precocious menstruation and puberty, it is very likely to be of the granulosa cell type. Again, if a tumor is found in a patient well beyond the menopause, associated with periodic and perhaps pseudomenstrual bleeding, it is almost sure to be a granulosa cell cancer. The likelihood is converted into almost absolute certainty if a diagnostic curettage yields a frankly hyperplastic endometrium. In both these groups, hormone studies are of even greater value than in the case of tumors encountered in patients during reproductive life.

**Treatment.**—The treatment of these tumors is of course essentially surgical. The extent of operation must be based upon the concept of the degree of malignancy of these tumors, concededly less than that of other ovarian neoplasms. Many patients have remained well after simple **unilateral salpingo-oophorectomy**, but the authors believe that such a conservative plan should be followed in only a limited group, in view of the fact that recent reports indicate a greater degree of malignancy than had been previously assumed. In *young patients* the **removal of the adnexa on the affected side alone** would seem permissible, but such patients should be carefully followed for evidences of recurrence. The more common case in which the patient has already lived all or most of her reproductive life would seem fully to justify a more radical procedure, *i e.*, **hysterectomy with bilateral removal of the adnexa**. This would certainly apply to the frequent cases seen *in women beyond the menopause*.

In view of the radiosensitivity of granulosal tissue to **radiotherapy**, it would be expected that these tumors should likewise be very responsive to this form of treatment, although only a few reports have been made on this point.

For the present it would seem wiser to restrict radiotherapy to the treatment of inoperable or recurrent tumors, or to combine it preoperatively or postoperatively with surgery in the treatment of removable tumors.

**PARTURITION. — BREECH DELIVERY.** — An analysis of 3301 breech deliveries in the hospitals of Brooklyn, N. Y., from 1926 to 1930, inclusive, was made by C. A. Gordon, R. Garlick and P. Oginz (*Am J Obst. and Gynec* 28: 140 (July) 1934). The problem was to determine, if possible, the relative importance of age, parity, duration of labor, size of the fetus, and whether or not it was wise to decompose or break up the breech in the course of labor.

In the total number of 3241 cases there were 21 maternal deaths, 10 primiparas and 11 multiparas, a total mortality for breech presentation of 0.6 per cent. Five of these deaths occurred from causes not directly associated with labor—lobar pneumonia (1), cardiac failure (2), acute yellow atrophy of the liver (1), and cerebral embolism (1). In the other 16 cases, death occurred from rupture of the uterus (3), pulmonary collapse (1), hemorrhage and shock (4), and septicemia (8).

Cases studied included 302 prematures, 53 cases with serious congenital defects, 40 macerated fetuses, and 230 cases of multiple pregnancy, in which 290 fetuses presented by the breech.

The 2601 cases in which the fetus weighed 2500 grams or more were studied from the standpoint of management and were separated into 4 groups.

The 1597 cases of spontaneous and assisted delivery showed a fetal mortality rate of 6.7 per cent, and injury to 32 babies, 2 per cent.

In 555 cases of extraction, a fetal mortality rate of 18.7 per cent was shown; and 28 babies, 5 per cent, were injured.

Four hundred and five cases in which the breech was broken up showed a fetal mortality rate of 28.9 per cent, 40 babies, 9.9 per cent, were injured.

Forty-four cases of Cesarean section showed that maternal mortality amounted to 11.4 per cent, and fetal mortality, 0.45 per cent.

One hundred and seventy-two patients had abnormal pelvises, and 94 gave histories of previous breech presentation.

Fetal mortality in 163 primiparas over 30 years of age and in 540 cases in which the fetus weighed more than 4000 grams, closely approximated the average fetal mortality of the entire series.

Prolapse of the cord in 97 cases showed a fetal mortality of 46.4 per cent.

In the entire series of 3301 cases there were 617 fetal deaths, a total fetal death rate of 20.3 per cent. Excluding 302 prematures, there were 458 fetal deaths, or 15.3 per cent. Deducting those with serious congenital defects, 53, macerated fetuses, 40, and twins, 290, there were 2616 cases in which the fetus weighed 2500 grams or over, with 332 fetal deaths, or 12.6 per cent. 61 per cent of these cases delivered spontaneously or with some assistance.

Fetal mortality and injury increased with extraction and was highest when the breech was broken up. Proper management is the most important factor.

**CHOLINE, FUNCTION OF, IN LABOR.**—F. Walker and D. N. Henderson (Canad. M. A. J. 30:158 (Feb.) 1934) discuss the function of choline in labor, *viz*, first, to neutralize adrenalin and, second, to stimulate the uterus. Choline is found in nearly all living cells. The commonest source is the adrenal cortex, where the quantity is 9 times as great as in the medulla. It is a parasympathetic stimulant, causing increased salivation, bronchial spasm, intestinal peristalsis and a fall in blood-pressure. It antagonizes adrenalin, inhibiting its action on bronchial spasm, on the rate of the heart and on the blood-pressure. One milligram of choline counteracts the pressor effect of a 0.25 mg. of adrenalin. As the amount of adrenalin in the blood rises, the quantity of choline also rises to neutralize its effect. The administration of atropine brings about the disappearance of choline from the blood. Blood from the suprarenal vein was shown to contain 1 mg. of choline per c.c. of blood. After the administration of pilocarpine this rose to 1.9 mg. per c.c. Choline chloride is the common form in which it is found. Several derivatives, more powerful in their physiological effect, have been cited and a series of compounds with increasing toxicity has been isolated. It appears that if the blood-pressure should rise very high, and cannot be checked by the available choline chloride, then one of the more powerful and toxic derivatives may be formed to meet the sudden demand.

Investigations have been made in which the choline content of the blood of the umbilical cord was estimated and the results correlated with the duration of labor and with the maternal blood-pressure in both multiparæ and primiparæ. It was found that the average choline content of the umbilical blood is higher in cases in which labor is of less than 10 hours' duration than in those in which it is longer than 10 hours. The explanation given is that the greater concentration of choline stimulates the uterus to stronger contractions and thus reduces the duration of labor. It was found that the duration of labor increased directly with the systolic blood-pressure up to 130 mm. of mercury in primiparæ and to 120 in multiparæ.

The choline content of the umbilical cord increased directly with increased blood-pressure up to 130 mm. The relation between the blood-pressure and the duration of labor is explained in part by the theory that the blood-pressure is due to the increasing quantity of adrenalin present in the maternal blood. This adrenalin seems to have a depressor action on the uterine muscle, weakening contractions and prolonging labor. When the blood-pressure is more than 130, labor is frequently shortened, and the explanation given is that choline chloride is probably not available in sufficient quantities to neutralize the effects of the adrenalin present, and more powerful choline derivatives are formed, especially the amino-choline substances with their toxic properties and effect on skeletal muscles, tending to produce convulsions.

**FUNNEL PELVIS.**—The incidence and importance of the funnel pelvis and a new pelvimeter for outlet mensuration is discussed by R. J. Pieri (Surg. Gynec. Obst. 59:891 (Dec.) 1934). A funnel pelvis is one in which the measurements of the inlet are practically normal, while one or more of the dimensions

of the outlet are smaller than normal. In general, any measurement which exhibits a decrease of 1.5 to 2 cm. below the average may be called contracted.

One of the chief etiological factors in the production of true funnel pelvis, it is now generally agreed, lies in the formation of the so-called "assimilation" pelvis. In 1900, Breus and Kolisko pointed out that the last lumbar vertebra, when fused with the sacrum, produces certain changes in the conformation of the bony canal. The sacrum, in this condition ("high" assimilation pelvis), is composed of 6 vertebræ instead of 5, while the lumbar spine is made up of but 4 vertebræ instead of the usual 5. Frequently, as a result of this fusion, both innominate bones are rotated on a horizontal axis in such a manner as to bring their lower portions closer toward the midline, thus narrowing the pubic arch and shortening the transverse (bisischial) diameter. According to various anatomists, assimilation, high or low ("low" assimilation, signifying 4 sacral and 6 lumbar vertebræ, and of little obstetrical importance), is the most common of all structural pelvic abnormalities. The condition is variously reported, from studies upon dried specimens, to vary from 21 to 38 per cent. in frequency.

For practical purposes, the normal diameters of the outlet may be taken from Table II as follows:

	Cm.
Transverse diameter . . . . .	10.0
Posterior sagittal . . . . .	7.5
Anteroposterior . . . . .	11.0

A point of great importance concerning these measurements is that forced flexion of the thighs upon the abdomen, with the woman either upon her back or upon her side, increases the distance between the symphysis and the tip of the sacrum from 0 to 4 cm., the average being 1.73 cm.

There are but two practical diameters, the transverse and the posterior sagittal. Of the total number of pelvises, 639, measured in this series, 69, or 10.79 per cent., presented some pelvic abnormality. Of these, 28, or 40.5 per cent., were of the funnel type.

The typical funnel pelvis signifies a pelvis in which the abnormality of the outlet contraction exists alone. The *prognosis* concerning the effect upon labor of various degrees of outlet contraction is not always obvious. However, as a general rule, if the transverse is more than 8 cm., no difficulty need be anticipated with a head of normal size. It is frequently observed that though the transverse diameter is contracted, the posterior sagittal may be normal or be proportionately increased, so permitting the uneventful passage of a full-term baby.

In making a prognosis in his cases, the author follows the general formula of the index mentioned, considering as normal diameters, however, a transverse of 10 cm. and a posterior sagittal of 7.5 cm. The normal outlet index then becomes  $\frac{10 \times 7.5}{2} = 37.5$  square cm. With this as a basis, experience has shown that the variations of the index as tabulated below hold true for the majority of cases.

Normal index of outlet, 37.5,	spontaneous
Index from normal to 30.0,	forceps occasionally
Index from 30.0 to 22.0,	usually forceps
Index 22 or less	practically obstructive

For measuring the transverse and posterior sagittal diameters a new instrument was devised. With this instrument both diameters of the triangle may be measured in one operation. No assistant is necessary. From the front, the instrument resembles an ordinary calipers, the arms and the tips of which are so constructed as to fit snugly against the ischial tuberosities in measuring the transverse diameter. A graduated scale on the anterior surface of the instrument records this distance in centimeters. The posterior arm of the pelvimeter is freely movable laterally and anteroposteriorly, and the distance (the posterior sagittal diameter) of its tip from the imaginary line (the transverse diameter) is recorded on a second graduated scale, regardless of the position in which the instrument is held. This second scale is also located on the front of the instrument.

In *contraction of slight degree*, so simple an operation as **mediolateral episiotomy** alone may provide the needed additional space. This type of incision, of course, avoids the rectum. With *increasing degree of contraction*, early **episiotomy and forceps extraction** are indicated to avoid needless protraction of the second stage of labor. And in using the forceps the mechanics of the blades and the physiology of the posterior triangle should be visualized. Rupture of the symphysis, as has been reported, through the use of the blades as a lever, is an obstetrical crime.

**INDUCTION OF LABOR.**—The induction of labor by **rupturing the membranes** is recommended by D. L. Jackson (Am J Obst and Gynec 27:329 (Mar.) 1934) from a study of 500 cases. If the cervix is flat or thin, when the membranes are ruptured, the beginning of labor is usually instituted so quickly and with such satisfaction that pituitary extract is not necessary. On the other hand, with the elongated noneffaced cervix, it can be expected that satisfactory labor will be delayed until the cervix is "taken up," when, as stated above, labor will assume a satisfactory rhythm, obviating the need of pituitary injection. It is probable that, if pituitary extract is given after rupture of the membranes, when the cervix is long, the effacement will be somewhat hastened but the authors believe that "whipping up" the uterus in this early stage of labor many times leads to distressing conditions, such as contraction ring and tonic contractions of the uterus. A little patience after rupturing the membranes, where the cervix is long, will allow the painless, constantly present, uterine contractions plus the pressure of the presenting part to efface the cervix, after which true labor will start.

*Routine.*—1. Patient enters the hospital at 8:00 P. M. on the evening before induction.

2. Is given **nembutal**, 3 grains (0.2 Gm.) or **luminal**, 1½ grains (0.1 Gm.) to insure a restful night.

3. **Castor oil**, 1½ oz. (45 c.c.) at 4:00 A. M.

4. **Quinine**, 10 grains (0.6 Gm.) at 5:00 A. M.

5. **Quinine**, 10 grains (0.6 Gm.) at 6:00 A. M.

6. Membranes ruptured at regular visit at 8:00 A. M. to 9:00 A. M.

The *technic* for rupture of the membranes has undergone only minor changes, and follows.

1. Patient is prepared and the vagina is filled with **hexylresorcinol**. This solution is used as the procedure requires no anesthetic, and hence, a preparation that does not irritate or burn is necessary.

2 A long hysterectomy clamp is easily slid along the examining fingers of the left hand and without force passed through the os uteri until its tip encounters the fetal head. The jaws of the clamp are opened slightly and then closed while held firmly, but not forcefully against the vertex. If the tips of the clamp close accurately, they will pick up the membranes, which rupture as the clamp is drawn outward. The examining fingers are held in the vagina throughout this maneuver, acting as a guide for the forceps in regard to both its direction and its relation to the presenting part.

3 All the fluid that can readily be released should be encouraged to escape

4. The patient is then put in the prone position and the fetal heart auscultated.

5. In the majority of cases, where the indications for elective induction have been properly judged, the uterus will show signs of contractions almost immediately. Where delay occurs at this stage or, in other words, where the latent period is prolonged, the judgment of the operator shall dictate whether he will use patience or pituitary extract. Labor will ensue in any event.

The patient is under observation throughout labor, and she is saved the anxiety of rushing to the hospital while in severe pain and having frequent contractions. If barbiturates or other hypnotics are used, they can be administered early for the patient's comfort. She also has had a night's sleep and is well rested when labor begins.

A Stem (Surg Gynec, Obst. 59:872 (Dec ) 1934) again emphasizes the value of the use of small dosages of **pituitary extract** in the induction of labor. His procedure is as follows

7 A M , castor oil, 1 ounce (30 c c ).

9 A M , pituitary extract, 2 minims (0.12 c c ) \*

10 A M , pituitary extract, 2 minims (0.12 c c ).\*

11 A M , pituitary extract, 2 minims (0.12 c c ).\*

Noon, pituitary extract, 2 minims.\*

The preparation of pituitary extract used during all these years is obstetrical **pituitrin**.

When labor pains start, the injections of 2 minims (0.12 c c ) are continued hourly. In successful cases, the pains generally begin after the second dose. If no pains are induced, the treatment is suspended and repeated on the third day succeeding.

It is to be regretted that the method has not found a wider application in the United States. Not one of the writers who have been reviewed has noted any evil effects upon either mother or child. In not one of the complicated cases, or even those in which fetal death occurred, could the outcome in any way be attributed to the use of the drug. The percentage of complications is, if anything, lower in the cases in which pituitary extract was used to induce labor than in those in which other methods of induction were employed, or even in those in which the pains occurred spontaneously.

It is to be hoped that American obstetricians will be inclined to employ the method more often as, combined with the judicious administration of nitrous oxide anesthesia in the second stage, it provides a safe and efficient means of delivery, which will go far to justify the continued demands of the modern woman that she be relieved of the age-old burden of the anguish of maternity.

\* By hypodermic injection deep into thigh

After 17 years' use, the author's technic has not been changed; and, in the opinion of those who have used it, it still remains the best procedure for inducing labor at term.

**PREMATURE SEPARATION OF PLACENTA.**—The *diagnosis* of premature separation of the placenta is not infrequently confused in the less severe cases with that of lateral placenta previa. If the two conditions are carefully distinguished, premature separation of the normally implanted placenta would appear to be a less frequent complication of pregnancy than placenta previa.

The type of *treatment* and the method of delivery are adapted to the circumstances of the individual case. **Cesarean section** is reserved for those instances in which the cervix is closed and the contraction of the uterus is ineffective in producing dilatation—where longer waiting means more bleeding.

Among 4246 obstetric patients admitted to the Jefferson Medical College Hospital during the 5-year period from 1928 to 1933 reported by T. L. Montgomery (Am. J. Obst. and Gynec. 28:33 (July) 1934) there were 16 cases of premature separation or 1 in 265 patients

One maternal death occurred in this series, a rate of 6.6 per cent. The fetal mortality rate was 81 per cent. Twelve of the 16 fetuses were premature

External violence is an infrequent cause of placental separation

Various degrees of placental separation occur not infrequently during the course of labor. They are produced by intrapartum attempts at delivery, or result from sudden decrease in the volume of content of the uterus

The most frequent etiologic factor in premature separation is toxemia of pregnancy. Particularly is it the predominating cause during the course of pregnancy, abdominal trauma accounting for only an occasional case

Nephritic toxemia is encountered more frequently in an etiologic rôle than is preeclampsia or eclampsia. There appears to be no reason for invoking the presence of some new or strange type of toxic disturbance to account for this complication

The characteristic lesion in the placenta in premature separation is hemorrhage. This may manifest itself in small or large areas of clot formation which push the placental villi aside. The compressed and crowded villi adjacent to the clot show early evidence of hyaline and granular degeneration. Interruption of pregnancy often follows, although the presence of old hematomas on the surface and in the substance of the placenta in cases of nephritic toxemia indicates that small hemorrhages frequently occur without causing a termination of pregnancy

The hemorrhagic lesions of premature separation are quite different in structure and etiology from necrosis (infarction) of the placenta

Necrosis (infarction) is found frequently in the placenta of both normal and toxic patients, its presence appears to play no part in the etiology of either placental separation or pregnancy toxemia

**UMBILICAL CORD COMPLICATIONS.**—Two groups of cord-complicated cases in the first stage of labor are distinguished by J. P. Gardiner (J. A. M. A. 102:277 (Jan. 27) 1934). The *first group* of cases is practically *symptomless*. The child is fatally asphyxiated from compression of the cord before the condition is recognized. The stopping of the fetal heart is the only

evident sign. It usually occurs during the first few pains in the first stage of labor, but may occur from a few hours to several days before labor definitely sets in.

It is the 100 per cent. mortality rate in such cases that gives grave concern. So unrecognized are the symptomless coilings in this first group of cases and so sudden is the fetal death that, at the present time, it is impossible to expect to save the life of the child by any method of delivery; yet it is not inconceivable to believe that if it was recognized that the fetal cord was being compressed and if delivery was immediately carried out, the child might be saved.

The *second group* of cord-complicated cases in the first stage of labor includes those which do *show symptoms*. The prognosis for this group is more hopeful, since there is a chance for the obstetrician to diagnose the cord complication and to save the life of the child. There are 3 cardinal symptoms that suggest a cord complication, *i. e.*, (1) delay in the progress of labor; (2) disturbance in the fetal heart rate; and (3) a malposition of the fetus. Pain at the placental site, a definite symptom due to traction, occurs later in the first stage, and in the second stage of labor. There may be, in a single case, all or only one of these symptoms.

**Treatment.**—The choice of treatment to be followed in cord-complicated cases is dependent on the diagnostic observations. It is only rarely that a **section** must be performed in any cord complication, but, when the indications point to a section, it must be performed in time to save the child.

“Amniography” consists of injecting from 10 to 15 c.c. ( $2\frac{1}{2}$  drams to  $\frac{1}{2}$  ounce) of some opaque solution, **skioldan** or **strontium iodide**, directly into the amniotic sac and after  $\frac{1}{2}$  hour (time for distribution) an x-ray picture is taken. In the x-rays, the cord as well as the position of the placenta can be outlined, and at times the sex can be made out. To be able to trace the cord in a cord-complicated case affords encouragement to proceed with more confidence in an outlined method of delivery. The x-ray picture is a permanent record which permits checking back on the technic of delivery in a manner not before possible. Gardiner has used it in a series of 8 cord-complicated cases.

**PREGNANCY.—COMPLICATIONS. — Anemia.** — Three groups of anemias are recognized, according to W. E. Studdiford (Am J. Obst and Gynec 28 539 (Oct) 1934)

(1) *Physiologic anemia* of pregnancy. The hydremia occurring in normal pregnancy results in an apparent small decrease in red cells and hemoglobin, but this is no true anemia. (2) *Microcytic hypochromic anemia*. This is characterized by a color index below 1, and a blood picture resembling a secondary anemia. The Price-Jones index, which is a curve constructed on the measured diameters of 500 red blood cells, falls to the left. It probably represents the results of iron withdrawals on the part of the fetus and responds well to iron medication. This type of anemia exists in from 30 to 40 per cent of all pregnant women. (3) *Macrocytic hyperchromic or primary anemia*. This is characterized by a color index above 1 and by a blood picture which resembles, and sometimes cannot be distinguished from, a true Addisonian anemia. The Price-Jones index shows the cells to average above normal in size, and so lies to the right of normal.



The first two groups are exceedingly common. The last group, while seen frequently in certain climates, is rare in the temperate zone.

**TREATMENT OF PRIMARY ANEMIAS.**—According to Studdiford, this will depend to some extent on their severity and upon the stage of the disease. The frequency of anemias of the secondary type in pregnancy should make the necessity of routine blood counts seem obvious. The most important time for the performance of blood counts would seem to be when the patient is first seen, at the seventh month, and shortly before term. In this manner the many secondary anemias and an occasional primary one would be discovered. If the diagnosis is made early, the anemia may be controlled by large doses of **liver extract** or **ventriculin**. Often intramuscular liver is more effective, particularly in cases with marked gastrointestinal symptoms. The patient can be carried along to a period of viability when, occasionally, Cesarean section may be indicated. Many of these patients show a deficient or absent hydrochloric acid in the gastric juice and should receive dilute **hydrochloric acid**. The gastrointestinal symptoms, which resist all direct methods of treatment, usually subside under **liver therapy**.

It must be remembered that it takes about 10 days for liver to show an effect on the blood count. In the more severe cases, therefore, and in those which are seen in the late stages of the diseases, **transfusion** should be used, and used repeatedly, if necessary. This is particularly important if evidence of an aplastic bone-marrow is present. A special indication exists at the time of labor because a crisis may occur shortly after this event. This procedure serves to tide the patient over the critical period before liver medication can take effect. The patient should be kept on liver therapy for at least 2 months postpartum. Finally, some patients seem to do better if **iron** is used in combination **with liver**.

**TREATMENT OF SECONDARY ANEMIAS**—( ) Richter, A. E. Meyers and J. P. Bennett (*Ibid.*, 28:543 (Oct.) 1934) discusses the treatment with **aqueous equine liver extract** and **glycerated iron**. Since these authors have previously shown that an aqueous equine liver extract and glycerated iron in defibrinated blood was beneficial in the treatment of secondary and hypochromic anemias, it was thought that treatment with this preparation might be of some benefit in the anemia of pregnancy. A careful analysis of 1½ ounces of this preparation, which was the average daily dose administered to the patients, shows that it contains the extract of 84.4 gm. of whole liver, a total of 104.24 mg. of metallic iron (6.75 mg. from liver, 5.62 mg. from hemoglobin, and 91.87 mg. from the neutral glycerol-iron compound), and a total of 1.4 mg. of metallic copper.

A summary of the blood changes occurring in the group treated with the liver, iron, and hemoglobin preparation, revealed that there was a gradual but progressive increase in hemoglobin and red blood cells. The erythrocyte concentration showed an average rise from 3.46 millions per c.c. to 3.95 millions at the end of term, with a corresponding increase in hemoglobin, which showed an average rise from 61 to 49 per cent. The color index remained about 0.8 throughout treatment. The average weight gain per patient during this interval was 31 pounds.

It was evident from these findings that the administration of the equine liver extract, iron, and hemoglobin preparation not only prevented a gradual reduction in hemoglobin and erythrocyte concentration during normal pregnancy, but

produced a reversal of this trend, and in the majority of patients a moderate increase in hemoglobin and red blood cells was obtained. This favorable response indicated that the anemia of pregnancy, at least to a certain degree, was due to a deficiency in the blood-building materials necessary for hematopoiesis

**Bronchial Asthma.**—Bronchial asthma occurring during pregnancy may be divided into 2 separate groups according to B. Green (J. A. M. A. 102:360 (Feb. 3) 1934) *viz.* (1) those in which a previous history of asthma can be obtained and (2) those in which the asthma seems to be a direct result of the sexual cycle or pregnancy. Group I includes those in whom the asthmatic attacks are directly traceable to sensitization to pollens, proteins or some focus of infection in the body, such as the teeth, tonsils and sinuses. In these patients a history of asthma antedating the pregnancy can usually be obtained, although occasionally the attacks made their first appearance during gestation. When they are encountered during pregnancy, the attacks are of much greater severity than usual, often reaching alarming proportions and terminating in the death of the mother or the fetus, or both.

The question of therapeutic abortion or induction of labor often arises in this type of case, but the consensus of opinion is that the asthmatic condition should be treated, *per se*, and the coexisting pregnancy ignored entirely.

Group II presents a varied and interesting series of cases in that the asthmatic attacks appear to be the direct result of malfunction of the female genital system. The cases may be divided into subgroups. In the first of these, the asthmatic attacks start with the menarche and recur with each succeeding menstrual period. Very often the attacks cease during pregnancy and lactation, only to recur on reestablishment of the menstrual cycle. It is likely that these attacks are precipitated by some of the hormones produced during the menstrual cycle or are due to absorption of some of the products of the uterine cavity during the phase of endometrial disintegration.

In another subgroup, the asthmatic attacks occur during gestation and lactation only. No history is obtainable of attacks antedating the pregnancy or after the termination of the pregnancy and lactation. Such cases are rare, but when they occur, indicate a sensitivity to some specific product eliminated by the embryonic tissue. This group is the only one in which therapeutic emptying of the uterus would be warranted in the hope of relieving the asthmatic condition. Occasionally, this group is found to subdivide into cases that show the asthmatic attacks during a pregnancy with a male fetus, with complete absence of attacks during gestation with a female fetus, and *vice versa*. It is possible that in such cases the factor responsible for the attacks comes from the developing sexual organs of the fetus.

**Eclampsia and Preëclampsia.**—BLOOD CHEMISTRY.—H. J. Stander and J. F. Cadden (Am. J. Obst. and Gynec. 28:856 (Dec.) 1934) present their findings of the blood chemistry in preëclampsia and eclampsia, which they regard as the same disease. Frequently repeated studies in 108 eclamptic and 40 preëclamptic patients show that the blood chemistry is an indispensable index of the severity of the disease and of specific treatment needed.

The nonprotein nitrogen content of the blood in eclampsia and preeclampsia remains within normal limits, except in certain instances, late in the disease when a rise indicates involvement of the kidneys as a result of the eclamptic disease.

The blood urea nitrogen remains low, as in normal pregnancy, with the result that the ratio between urea nitrogen and nonprotein nitrogen is about 0.4, as compared with 0.5 in normal nonpregnant individuals

The blood uric acid is increased in eclampsia and preeclampsia, indicating, it is believed, a disturbance in its destruction in the liver. The uric acid content in the blood may be regarded as a fairly safe criterion of the severity of the disease.

The blood sugar in eclampsia and preeclampsia is not greatly disturbed. Occasionally, a definite hyperglycemia follows an eclamptic convulsion, due perhaps to muscular activity

The alkali reserve is often greatly increased in this disease, sometimes even to the level of true acidosis. The  $\text{CO}_2$ -combining power is the best and most readily available index of the necessity of anti-acidosis treatment

The blood chlorides are not markedly decreased, except in an occasional patient with marked edema

Blood thionine values in eclamptic patients are within normal limits

Glutathione is similarly within normal limits, except in patients with low blood hemoglobin readings

The increase in blood uric acid in eclampsia and preeclampsia cannot be accounted for by an increase in thionine

The hyperglycemia sometimes observed in the convulsive state of eclampsia appears to be a true hyperglycemia and not due to glutathione or thionine

**SYMPTOMS**—T. Heynemann (*Ztschr. f. Geburtsh. u. Gynak.* 109:1 (July 27) 1934) claims that eclampsia and preeclampsia do not differ in their essential nature, but are the same, the differentiating sign being a single clinical symptom, the convulsions. The clinical difference is usually only one of degree

**DIAGNOSIS**—Formerly the diagnosis was based mainly on subjective symptoms, such as headache, visual disturbances, nausea, vomiting, dyspnea, asthma, accelerated breathing and increased depth of respiration. The author finds that headache is the most frequent and occasionally the only symptom and advises that headache, occurring without fever, should be considered a preeclamptic symptom, unless some other cause can be found. He shows that disintegration of the blood (hemoglobinuria and hematinemia) and development of hepatic disturbances (icterus and increased bilirubin content of the blood) indicate preeclampsia, particularly in case of edema and renal changes. However, the majority of cases of preeclampsia lack these symptoms. Changes in the fundus of the eye (form and size of vessels) are present in some patients. The results of vascular spasms are observable also in the capillaries of the nail groove, but their utilization for the diagnosis of preeclampsia is possible only with certain limitations. The epinephrine probe test of Muck is nearly always positive, but, since it is frequently present in patients without eclampsia and preeclampsia, its diagnostic significance in eclampsia is limited. Greater importance may be attached to the facial edema, for it is present in nearly all women with eclampsia and pre-

eclampsia. Anxious restlessness of parturient women is often the most prominent preeclamptic sign. The increase in the depth of respiration is likewise typical for preeclampsia. Then there is the reduced galvanic irritability of the median nerve. The increase in the blood-pressure is one of the most important signs, because it is generally the earliest indication of a preeclamptic state. A decrease in the quantity of urine and a considerable increase in the protein content are also signs of a beginning eclampsia. In some instances a sudden impairment of the general condition is the only indication of preeclampsia. If this symptom appears, the possibility of vascular collapse, cardiac weakness, rupture of the uterus, internal hemorrhage or preeclampsia should be considered. Premature detachment of the placenta in case of a normal site of attachment is not always a sign of preeclampsia. The author points out that in cases with indefinite signs the diagnosis may be difficult, but he emphasizes that a too frequent diagnosis is less dangerous than the failure to recognize eclampsia.

**TREATMENT**—At the first appearance of preeclamptic symptoms, **venesection** should be done. The first withdrawal should not be less than from 300 to 500 c c. If after this the preeclamptic symptoms do not disappear, the venesection should be repeated, or delivery by **Cesarean section** should be done at once, provided **forceps delivery** or **version** is not feasible. If icterus, greatly increased bilirubin content of the blood, changes in the fundus of the eye and stupor indicate a serious condition, **Cesarean operation** should be done at once. Hypertension as such does not necessitate abdominal delivery, but, if it persists in spite of treatment, prompt delivery is advisable.

L. G. McNeile (J. A. M. A. 103:548 (Aug 25) 1934) reports a study of 540 *preeclamptic* patients, of whom 35 developed convulsions (6.41 per cent), and of 259 patients with convulsive toxemias, a total of 799 cases.

#### ***Routine Treatment of Preëclamptic Patients:***

1 **Absolute rest in bed** is necessary. **Hospitalization** is very desirable, but patients with mild toxemias can be cared for in the home if hospitalization is not feasible.

2 A **milk diet** is used. In conformity with opinions expressed by many authors regarding nephritic, basic, and other diets in cases of toxemia, several types of diet have been tried from time to time. From the clinical standpoint an intake composed exclusively of milk and water is advantageous.

3 The **fluid balance** must be **maintained** by accurately measuring the fluid intake and output. If necessary, a retention catheter is used to insure the accurate measurement of urine excreted. Fluid bowel movements should be measured.

4 The bowels are to be kept active, 1 ounce (30 Gm.) of **magnesium sulphate** being given every 6 hours until the bowel movements are watery, then  $\frac{1}{2}$  ounce (15 Gm.) daily. The recent observation of A. D. Hirschfelder (J. A. M. A. 102:1138 (Apr 7) 1934) that in patients with renal insufficiency the oral administration of magnesium sulphate may produce coma, but that **sodium sulphate** may be substituted safely in such cases, may be the basis for changing this part of the treatment.

5. A urinalysis of a 24-hour specimen is made daily. A quantitative estimation of the albumin is done with a routine chemical and microscopic examination.

6. The blood-pressure is taken 3 times a day, or oftener if indicated by a rising blood-pressure or other evidences of an increasing toxemia.

7. Twenty c.c. (5 drams) of a 10 per cent **solution of magnesium sulphate** is administered intravenously when the systolic blood-pressure is 150 or higher and is repeated when indicated by a rising blood-pressure or other evidences of increasing toxemia. From 60 to 120 c.c. (2 to 4 ounces) may safely be given in 24 hours.

8. **Dextrose**, 300 c.c. (10 ounces) of a 25 per cent. solution, must be given intravenously from 1 to 4 times daily and is particularly important in patients showing decreased urinary output with or without a low carbon dioxide combining power of the blood.

9. Patients who are very restless should be given **chloral hydrate**, 20 Gm. (5 drams), and **sodium bromide**, 60 Gm. (2 ounces), by rectum.

10. If the symptoms improve, the author adds a **basic diet**, and places the patient on a very restricted regimen. If the symptoms do not improve, or become more severe, after a reasonable period, which, in this clinic usually varies from 4 to 7 days, but in not exceptional cases may be continued much longer, he ordinarily induces labor by **artificial rupture of the membranes**, or with a **Voorhees bag**.

**Cesarean section** is rigidly reserved for cases in which it is definitely indicated for some obstetric condition other than toxemia of pregnancy, and for patients with fulminating toxemia.

#### ***Management of Patient with Convulsions:***

1. Twenty c.c. (5 drams) of a 10 per cent **solution of magnesium sulphate** is administered intravenously as soon as possible after the first convulsion. This dosage is repeated every hour until the convulsions are under control. The subsequent dosage is based on recurrence of convulsions, elevation of blood-pressure and other signs.

2. The patient is placed in a private room. An attendant is with the patient constantly.

3. Inhalations of pure **oxygen** are administered to the patient after such convulsions and are continued until the respiration is normal.

4. If the patient is in labor, **nitrous oxide** or **ethylene analgesia** is given during contractions if the restlessness cannot be adequately controlled by **rectal administration of chloral sodium bromide**.

5. Self injury is prevented, if necessary, by using very **gentle restraint** during the convulsions.

6. **Absolute quiet in a dark room** is maintained and examinations are made only when absolutely necessary.

7. The general orders applying to the routine treatment of preeclamptic patients are continued so far as possible. The administration of **dextrose** is of great importance, as is also the **rectal administration of chloral sodium bromide** to patients who are restless.

8. If the patient is in the second stage of labor and progress is not being made, she is delivered with **forceps** or by other indicated procedures.

9. **Cesarean section** is done only for a *bona fide* obstetric indication or for a fulminating toxemia, and then only with the consent of the senior attending obstetrician.

The author is convinced that many reports criticising the use of magnesium sulphate in eclampsia, because of ineffectiveness, have arisen because an adequate dosage was not used. During the first 5 years of its use the dosage was constantly varied. It is the opinion of the writer that, in general, the dosage recommended is clinically safe and effective and that the use of smaller doses is not likely to give satisfactory results.

The continued use of the drug over long periods of time in preeclamptic patients who do not show definite improvement is not to be recommended.

W. Stroganoff, of Leningrad (J. Obst. and Gynec. Brit. Emp. 41 : 592 (Aug) 1934), advocates the **early rupture of the membranes** in the treatment of *eclampsia*. By early rupture he means when the os is closed or not larger than 2 inches (admitting 2 fingers). It is obvious that the membranes should not be ruptured if there are any contraindications, such as transverse position or presentation of the funis.

The first point of note was the rapid delivery which followed rupture of the membranes. Even when labor had not commenced, delivery occurred within an average of 22 hours 6 minutes, in 7 cases out of 18 the period was 12 hours or even less. When the os admitted from 1 to 2 fingers, delivery was observed to occur on the average within 9 hours. The majority of patients were primiparæ (74) and only a small number (12) were multiparæ. These data serve to prove that early rupture of the membranes is a valuable means of treating severe cases of preeclampsia and eclampsia. In his collective experimental series of 380 cases he has not had a single case of Cesarean section. Out of a total of 1800 eclamptic cases, he has agreed to only 2 vaginal Cesarean sections being performed. In 50 out of 87 cases, not a single fit was observed to occur prior to delivery following rupture of membranes, out of this number, 3 patients had fits subsequent to delivery. The number of fits in the case of the other patients was fairly small. It is of interest to note that in preeclamptic cases, very severe cases exclusively, the effect of the operation was also most favorable—only 2 patients out of 6 had fits prior to delivery, and 4 had fits only after delivery.

Following the discharge of 150 to 400 cc of the liquor amnii, the uterus becomes smaller and the pressure in it is lessened; and, further, the absorption of liquor amnii containing certain ferments and extractive substances into the mother's circulation is thus reduced.

Together with the decrease in the size of the uterus, the contents of the abdominal cavity are also reduced in volume and the intraabdominal pressure in it is lowered, at least for a certain period of time, which results in the abdominal organs being better supplied with blood. Besides, the diaphragm descends somewhat lower and its excursions become less restricted, oxidation of the blood is improved and all the organs of the body, and especially those of the abdominal cavity, come under better conditions of nutrition and respiration. The heart will

also be working under more favorable conditions, owing both to the shifting of the diaphragm and to the reduced intraabdominal pressure. It is true that the changes are very small, but their importance can hardly be denied. It may be that nervous and, especially, vasomotor reactions to the rupture of membranes, with all their consequences, are of still greater importance.

Like other methods of surgical interference, this one may also have its drawbacks. In the first place, there is the possibility of infection, although this is certainly less than that of recurring fits and very much less than the danger accompanying Cesarean section.

In *eclampsia intragraviditatem* he is guided by the same principles and the patient's general condition; high blood-pressure and the function of the kidneys are of prevailing importance. Generally speaking, he endeavors in the milder cases to stop the fits and allow the pregnancy to continue, and very frequently he succeeds in achieving the desired result. If in a case of *eclampsia intragraviditatem* the patient develops 3 fits in the hospital, in spite of the prophylactic treatment, he considers **rupture of membranes** to be indicated. Likewise, he interrupts pregnancy in cases in which after the fits have ceased there is not any improvement in the symptoms of eclampsism within the next 3 to 6 days.

In *intrapartum eclampsia* he **ruptures the membranes** in those cases in which venesection is indicated, *i e*, in patients who have had no less than 6 fits previous to admission, or in those who have had 3 or even 2 severe fits in the clinic, in spite of the prophylactic treatment being applied.

The technic consists in dilating the cervical canal with Hegar's dilator up to number 18-23 and then rupturing the membranes with the finger, or more often with one blade of a volsellum and cautiously widening the rupture so as to cause the least possible trauma. When the os admits one finger or more, the use of dilators is unnecessary.

**Hemorrhage.**—A discussion of the *prevention of maternal mortality from hemorrhage* is given by P. Brooke Bland (Pennsylvania M J 37:470 (Mar) 1934)

(a) *Ectopic Pregnancy*—With a history of menstrual irregularity, together with slight uterine enlargement, and a movable, almost tenderless, pulsating, oval mass lateral to the uterine body, the diagnosis becomes transparently clear. With rupture or abortion of the pregnant tube, the antecedent history, linked with the immediate alarming symptoms, presents a vivid clinical portrait.

If, in spite of the clinical picture, so clearly drawn, there still remains a diagnostic doubt, confirmation is readily afforded through an incision in the posterior vaginal fornix. This releases at once a quantity of accumulated blood in the dependent retrouterine pouch.

With the condition recognized before, during, or after rupture, the indications for treatment are plain. A pregnancy outside of the cavity of the womb is especially a **surgical** condition; and the only **treatment** worthy of consideration.

(b) *Hydatidiform Mole*—With the diagnosis of hydatidiform mole established, no policy save active interference with **prompt removal** of the mole can be looked upon in the light of preventive therapy.

(c) *Placenta Previa*—From its very beginning, placenta previa is a surgical emergency and it should be so treated. Just so long as the placenta, partly attached and partly detached, is allowed to hang over or about the internal os, just so long will the bleeding not only continue, but will tend to grow rapid and threatening in volume.

In no instance should meddlesome manipulation, as, for instance, packing or plugging the cervix with the fetal buttock, or any other temporary expedient, be practiced.

(d) *Premature Separation of Placenta*.—Though numerous causes, such as trauma, inflammatory lesions of the endometrium, multiparity and neoplasms, have been mentioned, it is now generally conceded that either nephritic or pre-eclamptic toxemia is responsible in nearly all cases.

Nephritis or nephritic intoxication complicating pregnancy must be treated, as recently emphasized by Stander and others, in a more active way. By adopting this course, the incidence of grave hemorrhage from premature separation would be diminished greatly.

(e) *Postpartum Hemorrhage*—Under no circumstances should efforts be made to extract or expel the placenta until the tired uterine wall fully reacts from its efforts to expel the fetus itself. This is not measured by time, or, as is frequently taught, in 15, 20, or 30 minutes. It is determined by the condition of the uterine musculature.

In all cases of postpartum hemorrhage, moderate or severe, the prevention of maternal mortality is further controlled, not by a passive attitude, but by **active stimulation**, the application of **heat**, the administration of **saline** or other **solutions** and by the direct **transfusion** of 400 c c or more of whole blood.

W. B. Hendry (Canad. M. A. J. 30: 629 (June) 1934) discusses the problem of hemorrhage in pregnancy and childbirth which holds third place among the causes of maternal death. At least half of these deaths are preventable. Hemorrhage in the first 3 months is usually due to one of 3 causes, *i. e.*, abortion, ectopic gestation, or hydatidiform mole.

The frequency of abortion equals 12 per cent of the cases going to term. More than one-third are admittedly self-induced. *Threatened abortion*, characterized by hemorrhage with a closed os, is treated by **rest in bed**, **sedatives** and a **small daily enema**, the patient being kept in bed for a week after the hemorrhage has ceased. Ergot is not given. *Inevitable abortion*, when pains are severe and regular, the cervix dilated, and the ovum presenting, is treated by **packing the cervix and vagina tightly with gauze** and by the administration of 5 grains (0.3 Gm.) of **quinine** and 3 grains (0.2 Gm.) of **ergotone** every 4 hours for 24 hours, at the end of which time the gauze is removed, usually accompanied by the ovum.

*Incomplete abortion* in the absence of fever is treated by **emptying the uterus under gas and oxygen**, **swabbing the uterine cavity with iodine** and **packing it tightly with gauze** for 24 hours. In the presence of fever, the treatment is conservative. Cervical smears are examined and a blood culture made. Indications for emptying the uterus are severe hemorrhage and the presence of



secundines Should **curettage** be necessary, care must be taken to avoid breaking down the layer of leukocytes Again the **uterus** is **swabbed with iodine** and **packed with gauze** for 24 hours

*Ectopic gestation* forms about 1 per cent. of pregnancies. Errors in diagnosis range from 15 to 30 per cent. In 5 per cent. of cases there is no history of amenorrhea and in a slightly higher percentage no vaginal bleeding. In 20 per cent. the hemorrhage is red, not dark brown in color, and in 30 per cent. the history and symptoms resemble those of threatened abortion. In more than 10 per cent. pain is referred to locations other than the lower abdomen. A temperature varying from 1° to 4° higher than normal and leukocytosis, proportional to the amount of blood in the peritoneal cavity, are seen in all but cataclysmic cases. Pain is so variable in character, degree and location that ectopic gestation must be considered possible in all acute abdominal conditions between puberty and the menopause. When in doubt, **posterior colpotomy** may be performed. Blood in the pouch of Douglas confirms the diagnosis. In all cases **operation** is imperative.

*Hydatidiform or vesicular mole* precedes 40 per cent. of all cases of chorionic carcinoma. It occurs once in 800 pregnancies. Vesicular degeneration of the chorionic villi begins early in pregnancy; at the twelfth week the uterus is as large as it is at the twenty-fourth week of a normal pregnancy, it is smooth, round and resilient. Fetal parts and movements cannot be felt. Nausea and vomiting are usually exaggerated until bleeding occurs, when they subside. The Zondek-Aschheim test is positive. When vesicles appear in the clots, the diagnosis is complete. The **uterus** should be **emptied and carefully curetted**, so that degenerated villi may not be left behind. It is **swabbed with iodine** and **packed with gauze** for 24 hours. The Zondek-Aschheim test should be made before the patient leaves the hospital, if positive, a second curettage should be carried out, and the patient should be kept under observation and treatment until the test is found to be negative.

*Premature separation of the placenta* must be considered a complication of the late toxemias and a possible source of danger in these. The hemorrhage may be revealed, concealed or both, and may be moderate or severe. It must always be regarded as a danger to both mother and child. It is accompanied by irregular painful uterine contractions, the uterus is tender and in severe cases tense and hard. Shock and collapse are out of all proportion to the visible hemorrhage. In all cases the patient is put to **bed** and treatment is directed towards combating the shock and arresting the hemorrhage. When the hemorrhage is revealed, the **cervix and vagina** are **tightly packed with gauze** and a **firm abdominal binder** applied. Labor may be induced by rupture of the membranes, (a) alone, or (b) aided by 0.5 c.c. (8 minims) of **pituitrin** given hypodermically, or (c) combined with the introduction of a **hydrostatic bag**. Usually labor begins readily and proceeds normally. At its completion postpartum hemorrhage is a real danger in all cases. The most dangerous type—that in which the placenta is completely detached, the fetus invariably dead, the uterus tense, distended and its walls weakened by intramuscular extravasation of blood and the patient in a state of collapse—is best treated by **Cesarean section** or **hysterec-**

**tomy**, together with **intravenous medication** and **blood transfusion**. **Cesarean section** alone is liable to be followed by postpartum hemorrhage.

*Placenta previa*, characterized by painless uterine bleeding, is to be suspected when the presenting part rides high and does not enter the brim. An abnormal thickness or boggyiness is felt in one or all of the fornices. If the os is dilated, the placenta or its margin may be felt. Radiography after injections of thorotrast is valueless, being incorrect in over 50 per cent of cases. The treatment is **rest in bed** under constant supervision until the pregnancy is terminated. Uniformity of procedure is not constant. The age and parity of the patient, the amount of hemorrhage, the location of the placenta, the condition of the cervix, the presentation and lie of the child, the presence or absence of disproportion and the stage of pregnancy or labor are all factors to be carefully considered. Hemorrhage before the onset of labor is treated by **packing the cervix and vagina with gauze**; in primigravidae with central placenta previa, **Cesarean section** should be performed.

When labor has started and the cervix is partially dilated, 3 methods are available (1) **rupture of the membranes**; (2) rupture of the membranes and the introduction of a **hydrostatic bag**; and (3) rupture of the membranes, **podalic version, pulling down a leg and attaching weight**. All three may be supplemented by 0.5 c.c. (8 minims) of **pituitrin**, injected intramuscularly. A plug to control the hemorrhage is supplied by these methods. The patient is given time to recover from loss of blood, and delivery should not be hastened. In the second stage, delivery is allowed to proceed normally, but may be assisted when there is urgency. *Postpartum hemorrhage* is liable to follow delivery of the placenta. Therefore, it is advisable to administer 0.5 c.c. (8 minims) of **pituitrin** at the end of the second stage and 1 c.c. (16 minims) of aseptic **ergot** at the end of the third. An **intrauterine douche** at 120° F. (48.9° C.) is given if the bleeding is excessive and the intravenous medication of **normal saline, glucose, gum-acacia** or **blood** is indicated. If the bleeding still continues, the **uterus is packed with gauze**. Constant watch is kept for the degree of uterine contraction, the height of the fundus, the quality and rate of the pulse and the amount of bleeding. Supervision is maintained for 48 hours.

*Pyelitis*—F. von Mikulicz-Radecki (Zentralbl. f. Gynak. 58: 1506 (June 30) 1934) cites 2 factors responsible for the development of pyelitis during pregnancy, *i. e.*, (1) the presence of coli bacteria in the renal pelvis, which results in bacteriuria, and (2) urinary stasis. It has been assumed by Stoeckel that, as a result of the toxins of pregnancy, the intestine and the ureters are in a state of atonia, and that because of this the coli bacteria can pass the intestinal wall more readily and enter the renal pelvis by way of the blood stream. The ureteral atonia results in a deficient urinary discharge and in urinary stasis, it favors the multiplication of microorganisms in the urine, the resorption of toxins and the invasion of microorganisms into the mucous membrane. It is possible also that the atonic ureter is more readily compressed by the growing uterus. On the basis of these opinions about the pathogenesis, the author stresses the following aims of the treatment: removal of the stasis in the colon and with it the coli invasion.

by **high enemas**; destruction of the coli bacteria in the urine by **bactericidal substances**; removal of the urinary stasis by counteracting the ureteral compression, by **having the patient lie on the side that is normal**, by increasing the urinary stream through the intake of **large amounts of fluid**, by **tonicizing remedies** and, finally, by drainage of the renal pelvis, *i. e.*, by **ureteral catheterization**. The renal pelvis permits not only a more exact diagnosis, but also a better treatment of the pyelitis of pregnancy. The author admits that ureteral catheterization does not always accomplish its aim, for it may prove impossible to push the catheter all the way up into the renal pelvis; nevertheless, it is effective in many cases. The obstruction is found most frequently in the subrenal ureteral loop, which is developed most noticeably during the second half of pregnancy. The author believes that by its bending, this loop becomes the cause of a sudden urinary stasis in the renal pelvis, which in the presence of a bacteriuria leads to pyelitis and, in case of sterile urine, to a typical pain underneath the kidney.

**Relaxation of Pelvic Joints.**—D. Abramson, S. M. Roberts and P. D. Wilson (Surg Gynec., Obst 58.595 (Mar ) 1934) discuss relaxation of the pelvic joints and particularly of the symphysis pubis as a normal accompaniment of pregnancy

Relaxation of the symphysis begins in the first half of pregnancy, progresses but slightly in the last 3 months, and is but little affected by parturition. Retrogression begins immediately following delivery, and is usually complete by the end of 3 to 5 months.

The process of relaxation is physiologic and is probably the result of a hormonal activity

Abnormal separation of the symphysis pubis occurs in about 25 per cent of the cases and probably results simply from an exaggeration of the normal physiological process, only exceptionally does trauma play any part

Symphyseal relaxation is accompanied by an increase of pubic mobility and is frequently associated with characteristic symptoms resulting from instability of the pelvic joints

Treatment is indicated to relieve symptoms and to prevent the development of a condition of chronic relaxation of the pelvic joints, which is frequently responsible for a great deal of later discomfort among women who have borne children

Prompt recognition of abnormal separation of the symphysis, when present, is essential and in order to detect this the obstetrician should include the symphysis pubis in his regular routine of examination of the pregnant patient, both antepartum and at the time of delivery

**Syphilis.**—An excellent summary of the present attitude toward the *diagnosis* and *treatment* of syphilis complicating pregnancy is presented by N. R. Ingraham, Jr and J. E. Kahler (Am J Obst and Gynec 27.134 (Jan ) 1934)

Syphilis in the latent stage, as it exists in most pregnant women, is difficult to detect. This means that the disease must be suspected in every case, for a successful termination of pregnancy and a healthy child cannot be expected in the presence of an active or even a quiescent infection of this nature.

The incidence of syphilis among pregnant women in the clinic class of patient is usually between 5 and 10 per cent. It occurs probably less frequently in the higher classes but, because it is less often looked for, more cases are likely to escape detection. In the presence of a comparatively early untreated syphilitic infection the infant mortality rate is increased to 5 times the accepted average.

Most authorities agree that syphilis runs a milder course in women than it does in men, but it has never been conclusively shown that pregnancy is the biological agency responsible for this change. There is some evidence that the disease may be activated by the added strain upon the maternal organism during parturition.

None the less, when the history and physical examination of the expectant mother are completed, it should be possible to suspect the presence of the disease, if the woman is infected, in from 25 per cent. to 64 per cent of cases, but in no instance should the blood serum Wassermann reaction be omitted. Since patients with infection of long standing, and those inadequately treated may give birth to a syphilitic child in the presence of a negative serologic examination, every child born deserves the benefit of a study to rule out this disease. In addition to the usual procedures, the umbilical cord blood is of value if all findings are properly interpreted and in this connection x-ray studies of the long bones are both reliable and valuable. It is wise to follow suspicious cases for some months at least.

The results obtained by early treatment of the syphilitic mother to save her child are scarcely paralleled in any other medical condition. An infected offspring is seldom encountered if therapy has been commenced prior to the fourth month of pregnancy. The observation that the *Treponema pallidum* does not traverse the placental barrier early, and the fact that antisyphilitic drugs only with great difficulty penetrate the membranes separating the maternal and fetal circulation, together emphasize the urgency of preventing infection of the child while there is yet time. For, once the microorganism has gained access to the fetal circulation, it is improbable that the fetus will be cured while still in the womb.

On the other hand, nonsyphilitic children, especially after adequate prenatal treatment, result with sufficient frequency to make it felt that the offspring should practically never be treated until the disease in him is demonstrated. This viewpoint is further strengthened when the prolonged course of active therapy with relatively toxic drugs that is necessary to insure a clinical cure of any syphilitic patient is considered. Treating an infected child for a few weeks postnatally cannot be expected to eradicate this disease.

In general, the pregnant syphilitic woman can undergo the same type of treatment régime as can the nonpregnant, but the technic of administration of the medication must be above reproach, and the dosage and type of drug gauged according to the condition of the patient.

The *outcome* of 943 pregnancies in known syphilitic women delivered under the supervision of the obstetric department of Johns Hopkins Hospital from 1914 to 1930 was studied by J. L. McKelvey and T. B. Turner (J. A. M. A 102: 503 (Feb. 17) 1934). The analysis was particularly concerned with the presence or

absence of congenital syphilis in the offspring, particular attention being paid to the effect of maternal antisyphilitic treatment on the outcome of pregnancy. In addition, the relative value in the diagnosis of congenital syphilis of such signs as the cord Wassermann test, placental histology, and x-ray examination of the infant's bones for syphilitic epiphysitis were considered. Among cases showing a negative cord Wassermann reaction, the infant was nonsyphilitic in 86.2 per cent., and among those giving a positive reaction, the infant was normal in only 18.6 per cent.

Among cases in which the placenta was normal on macroscopic and microscopic examination the infant proved to be nonsyphilitic in 79.9 per cent., while among cases showing syphilitic changes in the placenta, the offspring was syphilitic in all but 12.1 per cent. When these two diagnostic aids were considered together, the information was of more value than when each was considered alone. Infants presenting evidences of syphilitic epiphysitis invariably exhibited other evidences of congenital syphilis. However, among children showing no abnormalities on x-ray examination, 20.5 per cent. were subsequently shown to have congenital syphilis.

*Treatment.*—The striking beneficial effect of **antenatal arsphenamine therapy** is shown by the fact that among pregnancies occurring in untreated syphilitic mothers the infant was born alive in only 54.1 per cent., and 64.5 per cent. of living offspring were syphilitic, while the administration of as little as 1 Gm (15 grains) or less of arsphenamine changed these figures to 89 and 27 per cent., respectively. Administration of larger amounts of arsphenamine or related products brought about a further reduction in fetal mortality and in the percentage of syphilitic offspring, until when as much as 4 Gm (60 grams)—from 12 to 14 injections—was given, no syphilitic offspring was observed. The administration of heavy metals, **mercury** or **bismuth compounds**, in addition to arsphenamine, enhanced the good results achieved with the latter alone. Better results were obtained when maternal treatment was started in the first half of pregnancy than when begun in the latter half. It was found particularly important, however, that the arsenicals be given in the 2 months immediately preceding delivery.

The results in cases treated before pregnancy and not during pregnancy were, in general, quite as good as when the mother was treated during pregnancy only. Here, however, the status of the syphilitic infection in the mother is probably the important factor.

Antisyphilitic treatment both before and during pregnancy yielded results superior to treatment during either period alone.

**Toxemias of Pregnancy.**—*DIAGNOSIS*—*Fetus, Determination of Size in Utero*—S. H. Clifford (J. A. M. A. 103:1117 (Oct 13) 1934) notes that the premature infant group (weighing less than 5 pounds) represents but 3 per cent. of the total births at the Boston Lying-In Hospital, yet contributes one-half of the neonatal deaths. This premature infant mortality, however, can be reduced by the simple method of delaying the induction of premature labor, whenever possible, until a viable baby can be assured.

Evidence has been obtained suggesting that the weekly gain in weight of the fetus *in utero* is 4 ounces (120 Gm.) during the seventh lunar month, 6 ounces (180 Gm.) during the eighth, and from 8 to 12 ounces (240 to 360 Gm.) per week during the ninth month. With each 8 ounce increment in bodyweight there is a striking reduction in the death rate.

The determination of the ideal moment for the elective termination of pregnancy in the individual case depends on the possession of reliable information concerning the size of the fetus *in utero*.

This writer (Surg. Gynec. Obst. 58:727 (Apr.) 1934) also reports a method of x-ray measurement of the fetal head diameter *in utero*. The occipitofrontal diameter is measured by means of a modified roentgenometric technic. This diameter serves as a reliable index as to the maturity of the fetus. The relation that exists between the occipitofrontal diameter and the birth weight has been established through a study of more than 600 newborn infants. A graph has been prepared incorporating these data. It is possible, therefore, from an x-ray determination of the fetal head diameter *in utero* to predict the minimum and probable birth weight, the age of the fetus, and the mortality to be expected.

In the severer grades of *toxemia* the situation may arise wherein it is safer for the fetus to take its chance being delivered as a premature infant than to run the risk of being stillborn, should pregnancy be allowed to continue. The risk to the fetus of being delivered as a premature infant may be determined from information as to its expected birth weight. In reaching a decision, this is compared with the chance of fetal death *in utero* as determined from an evaluation of the severity of the toxemia.

In pregnancy complicated by *heart disease* without failure there appears to be little danger of intrauterine death of the fetus, and pregnancy may be allowed to continue as far as the maternal condition will permit. It is important to the future of the fetus that delivery should not be delayed until congestive failure develops, for under these circumstances the premature infant mortality mounts to 80 per cent.

When pregnancy is complicated by *slight vaginal bleeding* it may be possible to delay diagnostic examination, with the attendant danger of inducing labor or precipitating hemorrhage, until such a time as a viable baby can be demonstrated by the x-rays. In the presence of gross bleeding, the sooner the fetus can be delivered, the better its prognosis.

The influence of knowledge as to the weight of the fetus *in utero* in the management of certain types of pregnancy is felt to have contributed to the reduction in the stillbirth rate to 47 in 1933 from a level of 69 per thousand deliveries for the preceding 10 years. It has been instrumental in increasing the incidence of premature infants born alive from an average of 27.6 for the preceding 10 years to 34.7 per thousand deliveries for 1933. Furthermore, the proportion of premature infants weighing from 4 to 5 pounds at birth increased from an average of 52 per cent for the preceding 10 years, to 61 per cent during 1933. Finally, the premature infant mortality dropped for the first time in 5 years from 35 per cent to 29 per cent.

*Kidney Function Test.*—A study of kidney function tests in relation to the toxemias of pregnancy is reported by J. F. Cadden and C. M. McLane (Surg. Gynec. Obst. 59:177 (Aug) 1934). These investigators studied the phenol-sulphonphthalein, creatinine excretion, and urea clearance tests in 23 cases of normal pregnancy and in 343 women suffering from one or other type of toxemia of pregnancy.

Of the phenolsulphonphthalein, creatinine excretion test, and urea, only the latter is sufficiently sensitive to differentiate chronic nephritis from the other toxemias of pregnancy.

The lower limit of normal for the urea clearance test is probably in the neighborhood of 70 per cent. normal.

The average urea clearance value for nephritis is 75 and 68 per cent normal for antepartum and postpartum, respectively.

Fifty per cent. of all the nephritic patients showed values below 70 per cent. normal.

There is no apparent relationship between blood-pressure and kidney function, as measured by the urea clearance test

There is no kidney impairment, according to the urea clearance test, in the low reserve kidney group

The average urea clearance values for preeclampsia and eclampsia are lower than those obtained in normal pregnancy

The authors recommend the urea clearance test as the most sensitive method so far devised to recognize early or mild nephritis. To be assured that a nephritic condition is being dealt with, it is essential that repeated 2-hour tests be performed.

**TREATMENT**—W. J. Dieckmann (*Ibid* 59:678 (Oct) 1934) discusses the treatment of the toxemias of pregnancy at the Chicago Lying-in Hospital over a period of 2½ years. During this time there were 6968 deliveries, exclusive of abortions. Of these, 438 or 6.7 per cent were toxemic. The general plan of treatment for the nonconvulsive toxemia of pregnancy is as follows:

*Rest*—Absolute **bed rest**, with the additional use of sedatives, such as **luminal**, **bromide**, **amytal**, etc.

*Diet*—Limitation of protein, fat, salt. The fluid balance is watched carefully. The urine should form at least 80 per cent of the intake. Types of diet. For the eclamptic the diet consists of fruit juices. This is an alkaline diet because of the high content of potassium and sodium. It can be maintained from 5 to 10 days and is used in severe cases. As a rule, no limit is placed on the intake unless there is some evidence of cardiac decompensation.

For the preeclamptic, the diet consists of protein (60 grams), fat (30 grams), carbohydrate (400 grams), and is salt poor.

For the patient with nephrosis, the diet is similar to that for the preeclamptic, except that the protein content is increased to 100 to 150 grams. This diet is used if there is a marked albuminuria (5 grams or more per 24 hours) over a long period of time. Rarely used during pregnancy.

*Drugs*—**Luminal** is given in doses of ½ to 1½ grams (0.03 to 0.1 Gm.) 3 times daily, by mouth, **sodium luminal**, in doses of 2 to 5 grams (0.13 to 0.3 Gm.), *subcutaneously*, 2 or 3 times daily, if convulsions seem imminent.

*Elimination*—**Magnesium sulphate**, 60 c.c. (2 ounces) of a 50 per cent solution, is given by mouth and not repeated. Enemata of 180 c.c. (6 ounces) of a 50 per cent. solution are

used if edema is marked **Cascara**, **phenolphthalein**, or some other mild cathartic for daily use.

**Edema**—Eclamptic diet is adhered to and the water balance maintained. Occasionally fluids are limited to 1000 c.c. (1 quart), or even 800 c.c. (1½ pints), per 24 hours. Salyrgan and novasurol have been of no value. **Ammonium chloride** or **nitrate** in 6 to 10 Gm (1½ to 2½ drams) doses daily has been of use.

**Oliguria or anuria**—The intravenous injection of **hypertonic glucose solutions**: Usually 500 c.c. (1 pint), of a 20 per cent solution, is administered over a period of from 30 to 60 minutes and repeated 2 or 3 times daily. Occasionally, 1000 c.c. (1 quart) of a 20 per cent. solution is used.

If the 20 per cent. solution fails to produce a diuresis, from 500 to 800 c.c. (1 to 1½ pints) of a 30 per cent. solution is injected 2 or 3 times daily.

In patients with anasarca or with cardiac decompensation, from 100 to 200 c.c. (3½ to 6½ ounces) of a 50 per cent. solution is injected 2 or 3 times daily.

**Gum acacia solution**: If a diuresis cannot be produced with glucose solution, the injection of from 500 to 1000 c.c. (1 to 2 pints) of a 6 per cent. acacia in normal saline is of value.

**Magnesium sulphate solution**: The slow intravenous injection of from 100 to 200 c.c. (3½ to 6½ ounces) of a 2 per cent solution is of value in producing a diuresis if glucose injections fail.

Venesection and plasmaphoresis are no longer used.

There were only 3 Cesarean sections, with a questionable indication for one, performed in 15 antepartum cases of eclampsia. The 1 maternal death occurred in a patient who walked to the delivery floor at 3 30 P. M., began having convulsions at 4 00, and died at 5 00 P. M.

Of the 438 toxemic patients, 90, or 20 per cent., gave a history of previous toxemia. Of 29 patients who gave a history of convulsions in a previous pregnancy, 26, or 90 per cent., had some evidence of toxemia in the present pregnancy.

In general, the rules which the author attempts to follow are:

If the pregnancy is less than 28 weeks' gestation, and, if after a period of from 7 to 10 days' observation, study, and treatment, the symptoms and signs continue or become worse, the pregnancy is terminated. If the patient has one child or more, advise against future pregnancies if postpartum studies indicate a permanently impaired cardiovascular renal system.

If the patient is seen after the period of 28 weeks' gestation, and, if after 7 to 10 days' observation and treatment, there is no improvement, the pregnancy is terminated. However, if there is any amelioration of the signs and symptoms with bed rest, diet, elimination, and sedatives, no interference is indicated. Many of these patients can be carried to term and delivered through the natural passage.

An increase in blood-pressure, in the amount of albumin or edema, a decrease in visual acuity or amaurosis, jaundice, or the development of an oliguria or anuria warrants immediate termination of pregnancy.

The occurrence of convulsions in association with other evidence of toxemia warrants the termination of pregnancy unless the fetus dies *in utero*.

Toxemias of pregnancy will always be encountered, but **proper rest, elimination, and diet** will reduce the incidence. Preconceptional, prenatal, and postnatal care are of the utmost value in lowering the incidence and mortality of toxemia.

**Prenatal Care**—**Weight-taking** is considered by V. J. Harding and H. B. Van Wyck (Canad. M. A. J. 30:14 (Jan.) 1934) to be an important means of detecting an incipient toxemia of later pregnancy. Gains up to 5 pounds a month



during pregnancy are to be considered normal. Toxemia rarely develops in this group. Gains of more than 8 pounds should arouse suspicion of toxemia. A **diet deficient in salt**, with a **restricted caloric intake** is indicated. The closest supervision should be exercised. *Albuminuria*, *edema* and *hyperpiesis* are preceded by gains in weight. The prevention and control of retention of water may avert a toxic process.

An increase of the mother's weight due to *obesity* is to be treated by a **restricted diet**. This will in no way affect the child, which develops normally, even if the mother is markedly undernourished. Cases of toxemia are seen in which the fetus shows massive *edema*, and it is probable that milder cases occur in the absence of obvious edema. The sudden postnatal loss of weight frequently seen in large babies is often due to loss of excess water. **Special dieting** in the prenatal stage, by reducing this fetal edema, may facilitate labor. The prenatal routine followed was to allow a normal diet and a normal intake of fluid during the first 3 months. The same was allowed during the second trimester, except that a moderate restriction in salt was advised, provided the patient did not gain more than 5 pounds a month. When the gain was more than this amount, a salt-free diet was prescribed and the caloric intake was definitely reduced. At the same time the patient was seen fortnightly, weekly or even more frequently, the urine being examined and the blood-pressure estimated. On this restricted diet a slowing in the rate of gain was observed and, in some cases, a certain heaviness in the appearance of the face would disappear, as well as various subjective symptoms, such as sluggishness and dullness.

Observations were made on 726 unselected cases. Of these, 62 had monthly gains of 8 pounds, or more. All the cases of toxemia occurred in this group, except one which was known to be a case of chronic nephritis. In all but one, a marked increase of weight preceded either albuminuria or a rise in blood-pressure.

**Vomiting, Pernicious.**—H. B. Atlee (J. Obst. and Gynec. Brit. Emp. 41: 750 (Oct.) 1934) is of the opinion that pernicious vomiting of pregnancy is always a neurotic manifestation. He contends that if this be true, it is necessary to show that the postmortem findings are the result of the vomiting. Persistent vomiting does two things, it causes starvation, and it induces a constant loss of gastric juice, i. e., body-fluids.

The author finds that (a) In animal experiments with starvation and constant loss of gastric juice it is possible to bring about changes in the liver practically identical with those found postmortem in pernicious vomiting of pregnancy. (b) There is evidence that starvation sensitizes the liver to damage by poisons that it can normally deal with without damage. (c) There is evidence that mental disturbance *per se* can produce fatty degeneration of the liver.

From this it would seem justifiable to claim that it is the vomiting, with its ensuing starvation and loss of gastric-juice, which brings about the pathological changes found in pernicious vomiting, and not these pathological changes which bring about the vomiting. In other words, the vomiting comes first and the pathological changes afterwards. The author points out why the vomiting is of the nature of a neurosis.

1. The fact that dramatic success attends so many varying types of treatment, based on such widely differing pathological concepts.
2. The fact that similar vomiting occasionally occurs in the husbands of pregnant women.
3. The fact that so many cases of persistent vomiting of pregnancy present clear evidence of psychological conflict.
4. The uniform success attending the treatment of the condition by suggestion.

TREATMENT.—The patient must be placed in a hospital; a promise must be obtained from the husband and all other relatives not to visit the patient until vomiting has ceased for 48 hours. The author keeps the relatives away because he found in earlier cases that their advent to the sickroom was often the signal for a fresh outburst of vomiting. This is especially true in regard to the husband.

It is not necessary in most cases to isolate the patient, although the writer has had to do so 3 times before vomiting ceased. His routine is as follows: From the moment the patient enters hospital, she is denied the solace of the vomit-bowl. She is told that, in the event of not being able to control herself, she is to vomit into the bed; and the nurse is instructed to be in no hurry about changing her. He sees these patients as soon after admission as possible and assures them very dogmatically that they are going to stop vomiting at once, and that they will leave the hospital perfectly well in a week. He tells them to eat whatever is put before them, and instructs the nurse in their hearing to give them a fresh meal in 20 minutes if they do vomit. From the beginning, they are put on full hospital diet, and their tray is in no way arranged to make them feel that they have digestive capacities other than normal. They are assured that the more they eat, the quicker they will get better.

They are not given drugs of any kind. In his earlier cases, the author did not give fluids intravenously, but now, if the patient is greatly dehydrated and the skin dry, the eyes sunken, he prescribes glucose and saline, in order to increase the body-fluids and help the smoking fats to burn.

The subsequent history of these patients was as follows: 15 ceased to vomit within the first 24 hours and did not vomit again; 4 ceased on the second day, 6 on the third, 2 on the fourth, 1 on the fifth day, and 3 continued to vomit until isolated. There were 4 failures, 3 who had to have the pregnancy terminated—1 of whom died, and 1 who died after developing pneumonia. They divide themselves into 2 groups: the 2 who had pregnancy interrupted and recovered, and the 2 who died showing obvious signs of having had severe hepatic damage. The author feels sure that his suggestion failed in 2 cases because he was not resolute enough, and had proof of this, as one of them returned 3 months ago to his wards pregnant again and “vomiting her head off.” He determined this time to put his conviction to a more resolute test, but, in spite of everything, the vomiting continued and the patient went downhill. Finally, when her albumin was plus 4, her pulse-rate 125, and her condition alarming, he haled her in desperation before a conference of the members of the hospital staff and asked them for their backing in continuing the treatment. Having obtained it, he then informed the patient that the entire hospital-staff had agreed that under no consideration could her pregnancy be terminated. Two days later, she was eating

full hospital meals and keeping them down. Her urine was normal on the third day, and her pulse-rate dropped to normal on the fifth. The patient had had no vomiting since

**DIAGNOSTIC TESTS IN PREGNANCY.—*Aschheim-Zondek Reaction.***—L. Davy and E. L. Sevringhaus (*Am J Obst. and Gynec* 28:888 (Dec) 1934) have made an analysis of errors inherent in pregnancy tests based on the Aschheim-Zondek reaction in 425 cases. A total accuracy of slightly more than 90 per cent of the series was attained. Three modifications were employed either as individual methods or as concurrent tests with interpretations of the results as a single test. Analysis of the data reveals that erroneous diagnoses, due to limitations inherent in pregnancy testing by these methods, were made in 8 per cent of the cases.

Such systematic errors occurred in 3.92 per cent of the pregnancies. Two were in very early pregnancies testing correctly positive later. In early pregnancies, more consistently accurate results were obtained by a modification of the Friedman rabbit test or by an immature female rat test than by the Schneider immature rabbit method. Incorrect negatives were obtained in 9 pregnancies of more than 1 month duration. In 7 of these there was definite fetal or maternal pathology, in 1 there was no known pathology, and in 1 the history was not reliable.

Faulty tests obtained in 12.7 per cent of the nonpregnant group may be classed as systematic errors. Many of the cases which gave false positive tests can be correlated with known gynecological problems in which there was demonstrable endocrine disturbance. Each of the cases testing incorrectly positive has been studied from the standpoint of the clinical features manifest before and after the test and with respect to the ovarian picture obtained in the injected animals. Correlation of the laboratory and clinical findings suggests that cases of ovarian dysfunction in the nonpregnant may be differentiated from pregnancy by the concurrent application of 2 or more tests to the urine. In cases of this type, false positives have not occurred with the use of either the Schneider immature rabbit or the immature female rats as test animals. The more highly sensitive Friedman rabbit is of value for the demonstration of gonad-stimulating substance in the urines of nonpregnant individuals.

***Fish Test.***—A. E. Kanter, C. P. Bauer, and A. H. Klawans (*J. A. M. A.* 103:2026 (Dec 29) 1934) describe their results with a new biologic test for hormones in pregnancy urine, employing female fish of a species that have an externally visible oviduct. This work is based upon the report in 1932 of Fleischmann and Kamm that female bitterlings show an enlargement of the ovipositor following injection of estrin hormone.

F. Szusz (*Monatschr. f. Geburtsh. u. Gynak.* 96:292 (Mar) 1934) had previously tested female bitterlings with boiled and unboiled urine from pregnant women, male urine, estrogenic substance (progynon and hogival), and anterior pituitary extract (glanduantin), 10 c.c. of each to 1 liter of water in which the fish are placed. During the breeding season 48 fish were tested and all showed lengthening of the ovipositor in from 36 to 72 hours with both the boiled and the unboiled urine. Six fishes tested with anterior pituitary extract showed

no changes. Urine from 20 nonpregnant females gave 12 positive and 8 negative reactions. Male urine caused some lengthening in 7 of the 37 tested, greater lengthening in 22 instances, and no reaction in 8. This author tested 22 fish from July 1 to August 15 and all gave negative reactions. Szusz does not know what is responsible for the reaction. He concluded that full lengthening of the ovipositor takes place in 72 hours, that the test can be positive only during the breeding season; that male urine may cause a positive reaction; and that a negative reaction during the breeding season is absolutely indicative of the absence of pregnancy.

Kanter and his associates (*loc. cit.*) felt that tests could not be conducted along scientific lines until the fish had been standardized, *i. e.*, it was necessary to know in advance whether each fish was capable of responding positively to urine from a known pregnant woman and that the same fish would not react to the urine from a patient who was not pregnant. After a positive test it requires from 14 to 20 days for the ovipositor to return to its normal length, during which time the fish cannot be used for testing purposes.

A previously standardized fish is put in a 2-quart bowl which contains 1 quart of water at the proper temperature, about 75° F. The fish is observed, to make certain that the oviduct is not beyond normal limits. Four c. c. of the urine to be tested is put into this water. The fish is observed at 24-hour intervals. If the test is found to be positive after the first 24 hours, the test is discontinued; if negative, it must be carried out for 72 hours before a definitely negative report may be given, in spite of the fact that about 80 per cent of positives were positive at the end of the first 24 hours. Normally, the oviduct is about 2 mm in length and reaches less than half the distance to the end of the ventral fin. With a positive reaction, the ovipositor reaches past the edge of the ventral fin or to a length of 15 to 25 mm. After the test is completed the fish is put into a tank for recovery and left for from 2 to 3 weeks in order to allow for the regression following the positive reaction. It may then be used for other tests.

Fish tests were run parallel to Friedman tests in order to determine their relative merits. Up to the present, the authors have 31 such tests, with 27 absolute checks and 4 discrepancies between the two tests.

The fish are primarily cheaper than rabbits or mice, are easier to maintain, because of the small amount of space, food and care required in their handling, and at the end of the test it is not necessary to operate on the experimental animal and destroy it, as the fish may be used repeatedly for testing purposes. Another point in favor of this test is the fact that most positive results are obtained in 24 hours, while the other tests must run from 48 to 72 hours.

**Friedman Test.**—A review 1137 Friedman tests performed at the Mt Sinai Hospital, New York, are reviewed by M. A. Goldberger, U. J. Salmon and R. T. Frank (*J. A. M. A.* 103:1210 (Oct. 20) 1934). Five c. c. of urine is injected in the morning and afternoon on 2 successive days and the ovaries are inspected grossly 48 hours after the first injection.

With the employment of this technic in 1093 intrauterine pregnancies, there were 6 false negative (0.55 per cent) and 1 false positive (0.09 per cent). The smaller percentage of error in the series is probably attributable to the one

essential point in which the technic used differs from that generally employed; *viz*, the use of 2 rabbits for each test. The value of using 2 rabbits is demonstrated by the fact that, in 22 of the first 635 cases, 1 of the two rabbits was negative in proved cases of pregnancy. This would indicate that at least 34 per cent of rabbits are refractory to pregnancy urine.

In 44 ectopic pregnancies in which Friedman tests were done in duplicate, there were 14 false negatives (32 per cent error). In this series, the Friedman test was considered to be of value only when it was positive. Not infrequently the diagnosis of ectopic pregnancy was made from the history and clinical observations, in the face of a negative test.

The high percentage of false negatives in ectopic pregnancy may be accounted for if the histologic structure of the specimens removed at operation is studied. In every one of the specimens examined there was either degenerated or necrotic villi. In 12 instances the villi exhibited various stages of degeneration, the majority being necrotic, appearing merely as "ghosts." In 1 instance there was a 4 months macerated fetus, in another, no villi were found. The latter specimen was reported by the pathologist as a "hematosalpinx, probably an old ectopic."

Of the 30 cases of ectopic pregnancy with positive Friedman tests, well preserved villi were found in the specimens of 22, villi in various stages of degeneration were found in 3, and no villi in 5 cases.

As the positive Friedman test is dependent on the presence in the urine of the anterior pituitary-like hormone elaborated in response to activity of the chorion, it is obvious that with death or degeneration of the chorionic villi the test will become negative. Keeping in mind the fact that quite frequently when the Friedman test is done in a case of ectopic pregnancy there has already occurred either tubal abortion or rupture, so that the chorionic tissue is either degenerated, dead or completely separated from the circulation of the host, the high percentage of false negatives becomes understandable.

In intrauterine pregnancy the Friedman test will become negative if there is either complete separation or degeneration of the chorion. On the other hand, with a dead fetus, as long as the chorion is preserved, the test will remain positive. The Friedman test was positive as long as 30 days after death of the fetus. Death of the fetus was determined by the disappearance of female sex hormone from the blood.

For the clinician, it is important to remember that a positive test means merely that the patient is excreting anterior pituitary-like hormone which is formed in response to the presence of viable chorion, that the positive test does not indicate whether the fetus is alive or dead, that the test will remain positive in missed and in incomplete abortions as long as viable chorion is attached to the uterine wall; and that a negative test does not exclude the presence of an ectopic pregnancy.

**URINARY TRACT IN PREGNANCY.**—H. P. Lee and W. F. Mengert (J. A. M. A. 102: 102 (Jan. 13) 1934) describe the effect of pregnancy on the urinary tract. The most striking change consists of a *dilatation of the ureter and kidney pelvis*, usually more marked on the right side; this phenomenon is so

common that it might well be said to be a normal concomitant of the pregnant state

This dilatation subsides rapidly after the termination of pregnancy, provided the pregnancy, delivery and puerperium are normal, and in many cases a marked decrease in the size of the ureters and pelvis can be demonstrated within 24 hours following delivery.

Abnormal delivery or an abnormal puerperium interferes with the return of the upper urinary tract to normal.

In 10 normal pregnant women, retrograde pyeloureterograms failed to show any evidence of obstruction anywhere along the course of the lower ureter.

In 15 normal pregnant women, draining the ureters with ureteral catheters for 24 hours, in order to overcome any obstruction that might possibly be present in the lower portion of the ureters, produced no change in the degree or character of the dilatation of the upper urinary tract.

With the exception of ovarian cysts and ovarian abscesses, pathologic conditions in the female pelvis do not cause dilatation of the upper urinary tract.

The authors disprove the theory of lower ureteral obstruction as the cause for dilatation of the upper urinary tract in pregnancy. They believe the condition is the result of some cause inherent in and peculiar to the pregnant state.

**PUERPERIUM.—CERVICAL EROSIONS AND ENDOCERVICITIS.—Treatment.**—A careful study at the eighth week postpartum showed unhealed cervical damage in at least 50 per cent. of all women delivered at the Woman's Hospital, New York, according to R. L. Barrett (J. A. M. A 103:1516 (Nov 17) 1934). It is the belief of gynecologists that unhealed cervical lacerations, chronic cervicitis and endocervicitis, with their subsequent structural changes, furnish a favorable site for the future development of cancer.

At the Woman's Hospital it was decided to treat a series of patients with damaged cervixes during the late puerperium. The method chosen was **electrocoagulation**. By its use heat is generated within the tissues, penetrating deeply enough to destroy the diseased tissue and to cause instantaneous thrombosis and so prevent hemorrhage. Electrocoagulation produces a complete cellular necrosis.

All treatments were carried out under local anesthesia of 2 per cent **nupercaine** applied topically on cotton pledgets. This has given very satisfactory local anesthesia, although when the coagulation is carried out high in the canal, there may be some complaint of uterine cramps. In the latter cases, it is advisable that a wide dilatation of the cervix should first be done.

The coagulation is easily and quickly accomplished by a sweeping motion over the entire diseased area, producing a white or grayish coagulum, carbonization, indicated by excessive sparking, being avoided at all times. The best results are obtained by light rather than deep coagulation, the penetration being, as a rule, from 2 to 5 mm.

All of the 120 patients have completed at least 3 menstrual periods since the treatment. In no case is there evidence of cervical stenosis.

Electrocoagulation, owing to its uniform penetration and destruction of diseased tissue without carbonization, is superior to cauterization in the treatment of cervical injuries in the late puerperium.

Healing, following electrocoagulation of the cervix, results in a smooth pliable epithelialized surface free from scar formation

**SEPSIS.—*Prophylaxis and Treatment.***—The prevention and treatment of puerperal sepsis is discussed by B. P. Watson (J. A. M. A. 103: 1745 (Dec 8) 1934). In studying the cases of febrile morbidity in the Sloane Hospital for Women, he finds that the three most commonly associated conditions are prolonged labor, extensive lacerations and excessive hemorrhage. General improvement will result only when it is recognized by every practitioner that a large number of obstetric procedures are of major surgical importance, that they can be undertaken with impunity only by one who has had special training, and that even in skilled hands the results will be disastrous if the procedure is attempted at the wrong time or in the wrong case

(1) When a puerperal patient shows an oral temperature of 100.4° F. (38° C) or higher on two readings at intervals of 4 hours, she is transferred to the isolation unit and individualized in all details of nursing care in one of the glass-screened cubicles in a ten-bed ward. (2) A thorough general examination of the throat, lungs, heart and kidneys is made. The uterus is palpated abdominally, the lochia is examined, a culture is taken from the vagina; and a blood culture is made. (3) If the uterus is tender and larger than it should be, an **ice-bag** is placed over it and the patient is given 3 oral doses of 5 grains (0.3 Gm) of **quinine sulphate** daily. (4) If the lochia is profuse or foul, the shoulders are elevated in the Gatch frame. (5) The **diet** is light and nourishing, a small **enema** is given daily and, if necessary, a **mild cathartic**, such as **magnesia magma**, is used.

In the majority of cases beginning in this way the condition is an endometritis, which may be due to a variety of organisms, with a probable preponderance of the anaerobic streptococcus. Most of these patients make a rapid recovery with no other treatment, so that in a few days the temperature falls to normal, the uterus begins to involute normally, and the lochia becomes less profuse and loses its odor. With this probable outcome, care is taken to do nothing that might favor an extension of the infection beyond the uterus. No pelvic examination is made other than to inspect any perineal lacerations and take a culture from just within the vaginal introitus. The uterus is not manipulated from the abdomen.

(6) If the patient shows a progressive anemia, or is losing ground, a **blood transfusion** of 400 c c is given by the direct method. This treatment is most important and may be repeated every 3 or 4 days, the amount given each time being from 250 to 400 c c.

The **operative treatment** of puerperal infections at Sloane Hospital is limited. A pelvic abscess is opened, but there should never be haste in exploring those massive cellulosic exudates which are sometimes found, until there is definite evidence of softening and fluctuation. Most of these exudates absorb without suppuration. The peritoneum is drained through the posterior fornix

or through a small incision above the pubes in cases of early peritonitis following septic abortion, and in the rare early case following full term delivery. The peritonitis developing late in a case of puerperal sepsis is usually just one expression of the wide hematogenous and lymphatic extension, and operation is useless. Never explore or curette the uterus in cases of septic incomplete abortion until the temperature has been normal for 3 days and it is known that the organism is not a hemolytic streptococcus. Cases in which there is excessive hemorrhage, the control of which may necessitate taking the risk of emptying the uterus, constitute the one exception to this rule. The author performs a hysterectomy in the rare cases of uterine abscess and of necrosis of a uterine fibroid encountered during the puerperium.

**PYELITIS.**—Atony of the musculature of the renal pelvis and ureter, with the resultant sluggish drainage of these structures, plays an important rôle in the development and course of pyelitis. The efficacy of drainage induced by ureteral catheterization in the treatment of this condition is well established. Unfortunately, however, this procedure requires a technical skill and specialized apparatus which are often beyond the resources of the general practitioner. For this reason, a simpler method available to any physician for accelerating the drainage of these structures would be of obvious value.

W. Darley and W. B. Draper (J. A. M. A. 102:677 (Mar. 3) 1934) report on the therapeutic value of posterior pituitary extract (**pituitrin**) in pyelitis. The series consists of 14 adults and 2 children and comprises 7 cases with no history suggestive of a previous pyelitis, 5 cases of recurrent pyelitis, 1 case of postpartum pyelitis, and 3 cases of postoperative pyelitis. All these patients presented the well-defined symptom complex that is characteristic of pyelitis.

In these 16 cases of pyelitis, renal pain of relatively prolonged duration was promptly relieved by solution of pituitary. The associated symptoms of fever, nausea, frequency and dysuria were also ameliorated, although in a less spectacular manner.

In their opinion, the results are due to accelerated drainage of the upper urinary tract induced by the solution. It is contraindicated in coronary disease.

**RAPE.**—An interesting discussion of the prevention of venereal disease and conception after rape is given in *Queries and Minor Notes* (J. A. M. A. 102:1782 (May 26) 1934).

Usually a case of rape is not seen for at least a few hours after the crime has been committed. At this time little can be done to prevent conception, because in nearly all instances in which conception takes place the fertilizing spermatozoon gains access to the uterine cavity within a few minutes after coitus. It reaches the Fallopian tube shortly afterward, but even if it did not, it is possible, though hardly likely, that a curettement performed when the patient is first seen will help. For a curettement to be effective in such a case, every bit of endometrium above the basalis must be thoroughly removed and also all the spermatozoa in the uterine cavity. Should a spermatozoon succeed in fertilizing an ovum in spite of a curettement, it is possible for the ovum to find a sufficiently prepared endometrium for embedding, because it usually takes



about 10 days from the time of coitus to the time of implantation in the endometrium. It may be dangerous to perform a curettement immediately after rape, because not infrequently the offender has gonorrhea. Smears should, of course, always be made of the vaginal contents to ascertain whether gonococci are present. If such organisms are found, a curettement is contraindicated. If the smears fail to show gonococci, this does not imply the absence of gonorrhea. The disease may not manifest itself until a number of days later. Evidences of syphilis will surely be absent if the woman did not have the disease before the rape was perpetrated, even though the offender has active syphilis, because of the incubation period of syphilis.

When a case of rape is seen, careful information should be obtained about the exact time of occurrence of the crime and a thorough examination made not only of the external genitalia and surrounding tissue, but also of the entire body for marks of violence. It is necessary for the physician to obtain this information, because he will undoubtedly be asked about these facts in court. Smears should be made of any discharge seen on the external genitals and also the contents obtained from the vagina. Careful notes should be made of the character of the vaginal contents, especially as to whether spermatozoa, blood and pus cells are present. Immediately after all the examinations have been made, the vagina should be irrigated with a weak mercuric chloride or potassium permanganate solution. Then the entire vagina, but especially the region of the Bartholin gland ducts, the cervix and the urethra, should be swabbed with a 2 per cent silver nitrate solution. In addition, one of the prophylactics used by men for syphilis, such as 33 per cent ointment of mild mercurous chloride, should be used on the external genitalia, in the vagina, on the external urethral orifice and on the cervix. Two weeks later, and again at 4 weeks, smears should be made from the cervix, vagina and urethra, and blood should be subjected to a Wassermann or Kahn test. If the blood test is positive, another test should be made to verify it. If the Wassermann or Kahn test is negative, 3 more tests should be made at intervals of 3 weeks.

As far as is known, no state in this country has made provisions for the induction of abortion in cases of rape.

**STERILITY.**—P. Brooke Bland and Arthur First (*Internat. Clin.*, Vol IV, Series 44, p. 197 (Dec.) 1934) discuss the modern concept of sterility.

**Investigation.**—In the light of recent research, a proper study of the female factors in the production of sterility, as carried out in the obstetrical department of Jefferson Medical College, includes:

1. A careful general and gynecological history.
2. A complete physical examination, with special emphasis upon endocrine and pelvic study.
3. Complete laboratory studies, including a serological blood test, a routine blood count, a urine examination, a basal metabolic rate determination, an estimation of the blood cholesterol, a premenstrual determination of the estrin hormone in the blood, an estimation of the pituitary blood hormone, a study of

the specific dynamic action of protein, a glucose tolerance test, eyeground and visual field examinations and an x-ray picture of the sella turcica.

4. A special gynecological examination, including a study of the endocervical secretions, a postcoital examination, a tubal insufflation and, if necessary, a subsequent lipiodol injection and a premenstrual curettage to determine the presence or absence of a normal premenstrual nadatory endometrium.

**Etiology.**—The factors responsible for sterility in the female may be divided into general causes, local causes, and functional disorders. Usually there are several abnormalities coexisting.

#### GENERAL CAUSES:

1. *Infections*—Both acute and chronic infections may exert a damaging influence on ovarian function and result in sterility. The acute infections, influenza, typhoid fever, mumps, scarlatina, tonsillitis and acute rheumatic fever may cause secondary ovarian infections and result in atrophy and sterility. The same is true of acute puerperal or other fevers. Focal infection may likewise be responsible for ovarian atrophy and sterility.

2. *Chronic systemic diseases* such as diabetes, renal, and pulmonary disease, or profound anemia, are not uncommonly associated with sterility, although these conditions are not absolute barriers to impregnation. Chronic alcoholism, morphinism and cocainism are also associated with sterility, while in organic and functional nervous conditions, impregnation is not likely.

3. *Consanguinity*—Sterility is not uncommon in the union of blood relations, although it is not an absolute barrier.

4. *Selective sterility* (incompatibility) refers to those individuals who do not bear offspring, although both may be fertile when united to other partners. This type is not frequent, but it does occasionally occur. The cause is not known. It, perhaps, resides in some biological process of natural selection not yet understood. Both partners may be of low fertility, although either partner may produce offspring in a highly fertile mate.

5. *Physiological Causes.*—Women are sterile during certain physiological states, as in pregnancy, except in those rare cases of superfetation in the normal or in the double uterus. Frequently women are sterile during lactation, although conception may occur during this period. Lactation sometimes is prolonged with a view to avoiding impregnation. Some women are sterile at certain periods (safe period) and for this reason the sexual relation is indulged in by these individuals only at this time. Physiologic sterility is, however, debatable. Knaus contends that women who menstruate every 26 to 28 days can only conceive from the ninth to the fifteenth day of the cycle, whereas those who bleed every 28 to 30 days are capable of fertilization only between the eleventh and seventeenth day of the cycle.

#### LOCAL CAUSES:

1. *Congenital Underdevelopment of Genital Organs*—One of the most common local causes of sterility—excluding the infections—is congenital ill-development of the genital organs, either in the form of a rudimentary vagina or uterus, stenosis of the vagina or cervix, or an imperforate hymen.

2 *Faulty Cervical Insemination*.—It is essential that the semen reach the cervical canal directly. Severe lacerations of the vagina, with prolapse of its walls, and of the cervix, allowing escape of the seminal fluid are provocative of sterility. Dyspareunia, resulting either from psychic conditions or lesions of the vulva and vagina, may be responsible. Urethral caruncles which are extremely sensitive may set up a vaginismus. Kraurosis vulvæ may not permit sexual access to be completed. Cervical infection with a pathologic cervical discharge is present in more than one-third of all sterile women.

3 *Hostility of Endocervical Secretion*.—Hostility of the cervical secretion is indicated when dead spermatozoa are found in this material 6 or 8 hours after coitus in women free from endocervicitis, especially if normal sperms at the same time are found in the condom specimen. This biochemical incompatibility is often associated with hypoplastic generative organs and precludes fertility. The hydrogen ion concentration of cervical secretion varies between 8.0 and 9.0 (*i. e.*, definitely alkaline). An excessively high acidity may occasionally cause sterility, although this is infrequent. The hostility of excessively acid vaginal secretion has been confirmed by conception occurring after neutralization or alkalinization of the vaginal secretion. The frequency of a highly acid secretion of the vaginal canal has, however, been overemphasized. Vaginal acidity is due to lactic acid which practically never exceeds 0.5 per cent. In this spermatozoa may live for hours.

4 *Displacements of the uterus* are seldom in themselves a cause, but they are sometimes indirectly responsible from the complicating inflammatory lesions of the lining membrane or the wall. It is now believed that uterine abnormalities are not important causes of sterility, although often accompanied by other conditions which render conception impossible. Thus, an infantile uterus may be associated with sterility because of infantile ovaries failing to ovulate. Acute anteversion is seldom responsible for sterility. The patency of the cervical canal may be instantly determined by the introduction of a sound with the thickness of from 2 to 4 mm., which is proof that no obstruction to the spermatozoa is present.

Symptomless retroversion of the uterus *per se* is not responsible for sterility. An exception to this is found in those patients in whom spermatozoa cannot be found in the cervix, although the vaginal secretions yield many. This may result from the anterior position of the cervix. Retroversion when associated, however, with chronic pelvic congestion and cystic ovaries, may at times be responsible.

5 *Tumors*.—Neoplasms of all types, especially those involving the endocervix or the endometrium as polyps, for example, may, if they develop early, result in absolute sterility, if later, relative sterility. Fibroid tumors are the most common forms of neoplasms associated with sterility. Submucous myomas, by obstructing the uterine ostia of the tubes, may prevent conception, or, by encroaching upon the uterine cavity, may cause abortion. Conception, however, may occur in fibroids of the interstitial and subserous type, especially if these are not complicated by endometrial, tubal or ovarian disease.

6. *Stenosis of Tubes*.—Partial tubal obstruction is a common cause of extrauterine pregnancy. Complete tubal occlusion is the most frequent cause of sterility. This may be the result of spasm, a developmental defect, or an antecedent inflammation. Acquired tubal stenosis is usually gonorrheal in origin, though it may follow abortion, appendicitis, peritonitis or intrauterine infections. Retroversion is cited as a common cause of tubal kinkage.

7. *Ovarian Sterility*.—This may be congenital or acquired. In the congenital type there is a retarded development of the ovaries closely associated with other endocrinopathic irregularities. In the acquired type, inflammation of the ovaries, resulting in hyperplasia or sclerosis, is not an uncommon cause of sterility. The antecedent pelvic infection, usually gonorrheal in origin, results in a thickened tunica albuginea which impedes maturation and rupture of the Graafian follicle. Failing to rupture, the follicles become the seat of cystic degeneration. In these patients there is invariably an associated endometrial hyperplasia producing prolonged menstrual flow. If ovulation does occur, an existing infarcted and hemorrhagic endometrium often prevents conception. Ovarian abscess due to gonorrhea or tuberculosis may cause complete destruction of the sexual glands. Ovarian cysts, by destroying the ovarian structure or by compressing the tubes, may likewise cause sterility.

8. *Contraceptives and Sterility*.—Various contraceptive measures resorted to in the first two years of marriage may produce hostile secretions and chronic pelvic congestion inimical to conception. The use, however, of intrauterine stems may well be considered as a cause, because of irritation, erosion and infection of the uterus and tubes. The use of strong vaginal antiseptics, as undiluted bichloride of mercury, may also be mentioned as causative.

FUNCTIONAL STERILITY.—Etiologically, cases of functional sterility are classified into primary pituitary, ovarian, or thyroid malfunction.

(a) *Primary Pituitary Deficiency*.—This condition, if not sufficiently severe to suppress totally ovarian function, is usually that of a mild Froehlich's type. These patients show genital hypoplasia, menstrual derangement, and distinct evidence of pituitary hypoactivity. These stigmata are a characteristic girdle obesity, hirsutes, with a male distribution of pubic hair, nervous stability, increased sugar tolerance, and a low specific dynamic action of protein. Often there are characteristic eye findings, consisting of contraction of the visual fields, yellow color of the discs, and enlargement of the "blind spots." There is no demonstrable quantity of anterior pituitary sex hormone in the blood in contrast to the finding in primary ovarian hypofunction.

(b) *Ovarian failure*, either primary or secondary to pituitary or thyroid deficiency, may result in functional sterility. The presence of a demonstrable quantity of anterior pituitary sex hormone in the blood (absent in normal fertile women) is the most significant finding in the diagnosis of a primary condition. These women are superlatively feminine, with visceroptosis and gastrointestinal spasticity.

Hypoplasia of the genital organs and menstrual irregularity or amenorrhea are frequent. They rarely show a normal level of female sex hormone in the blood at a time when 94 per cent of normal fertile women show a demonstrable

quantity of the hormone. In ovarian hypofunction the opportunity for fertilization is diminished in direct proportion to the reduced number of periods per year. Rubin found menstruation habitually delayed in 10 per cent of patients whose marriage was sterile. In 77 cases of oligomenorrhea sterility was present in 30 per cent.

According to Frank, many sterile women have a uniformly low premenstrual blood threshold level, as manifested by a diminished quantity of sex hormone, so that the uterine mucosa does not have the proper endometrial preparation necessary for successful nidation. In a study of 103 women with functional sterility, Mazer encountered 37 patients who menstruated regularly, 5 who menstruated scantily but regularly, 27 who had intervals of less than 3 months or more. In the group of 37 regularly menstruating sterile women, 22 showed no demonstrable quantity of female sex hormone in the blood near the time of an apparently normal menstruation, and 20 failed to exhibit a premenstrual endometrium. Such a type of menstruation, if constant, would preclude fertility.

(c) *Thyroid Derangements*—Thyroid failure in the adult female, either as a hypo- or hyperactivity, produces no palpatory evidence of genital atrophy, yet is occasionally the cause of infertility. The endometrium is hyperplastic and gives rise to amenorrhea and prolonged bleeding when menstruation does occur. Repeated abortion may be an expression of, or consequent upon, thyroid failure. The diagnosis is relatively easy if basal metabolic readings are resorted to routinely in the study of functional sterility.

**Treatment.**—A thorough knowledge of the etiological factors involved must be obtained before any course of treatment is outlined. For this reason the cooperation of the gynecologist, urologist and internist in a well-organized sterility clinic is essential for a proper study of the problem.

Lesions responsible for sterility are extremely varied and each case, therefore, must be studied individually, the cause determined and treatment, either medical or surgical, appropriately applied.

*Regulation of Sexual Act*—A failure to conceive may be due to the escape of the semen immediately after intercourse, due possibly to a relaxed introitus. This difficulty may be corrected by the knee chest posture or by placing a large pillow under the buttocks before coitus and remaining in this position for an hour afterwards. Conception is more frequent after coitus following ovulation, i. e., in the period 12 to 15 days after the beginning of the menstrual flow, which is also the ideal time for artificial insemination. Knaus claims that in women with a regular menstrual cycle of 28 days, conception can take place only from the eleventh to the seventeenth day of the menstrual cycle. Nevertheless, the sperms may live for some time in the generative tract before the ovum appears for fertilization, although it is generally conceded that they are not capable of fertilization for more than 48 hours. Ovulation induced by coitus may possibly occur in women, although thus far it has not been proved.

If hyperacidity of the vaginal secretions exists, this should be neutralized or alkalinized by the administration of an **alkaline douche** preceding coitus, using bicarbonate of soda  $\frac{1}{2}$  ounce (15 Gm.) to 2 quarts (2000 c c) of warm water.

*Diet.*—Recently, diet has received considerable attention in the treatment of sterility, due chiefly to the investigations of Reynolds and Macomber. These observers report that a diet low in calcium has considerable effect in reducing fertility and may even favor miscarriage. A **high protein and vitamin E diet, low in calories**, with the administration of **calcium lactate** and enough **exercise** to assure assimilation, is recommended. Diet is also of great value in the treatment of associated anemia or obesity. While obesity may not be the cause of sterility, it is frequently associated with evidences of diminished ovarian function which is improved by weight reduction.

*Tubal Insufflation.*—The Rubin test as a therapeutic measure has recently been brought to the fore. Pregnancy may follow insufflation by separating mild agglutinations and straightening tortuous tubes.

**TREATMENT OF FUNCTIONAL STERILITY.—Prophylaxis.**—In the treatment of functional menstrual disorders, prophylaxis in the adolescent youth is of utmost importance.

*Organotherapy.*—The correction of menstrual irregularities is of prime importance in the treatment of sterility. In the administration of endocrine products, the physiology of the ovary and pituitary gland must be borne in mind. **Desiccated thyroid tissue** in small doses tends to increase cellular activity throughout the entire body, including the endocrine glands, and hence is a most valuable adjuvant in the treatment of functional sterility.

**Estrin hormone therapy** causes an increase in growth and vascularity of the uterus, and renders it, therefore, more responsive to ovarian stimulation. Orally, estrin is one-fifth as potent as when administered subcutaneously. When estrin is given in divided doses over a 24-hour period (200 rat units daily), it is not so rapidly eliminated through the urine and is, therefore, better concentrated in the uterine mucosa. It is quite efficacious because of the marked stability of the hormone to strong bases, acids, and artificial digestion. The dose of estrin should be between 1200 and 2000 rat units daily, if taken by mouth over a period of 3 months until the uterus has acquired a normal size.

Theoretically, estrin therapy should be combined with injections of the **corpus luteum hormone (progestin, lipo-lutin)**, especially for regularly menstruating sterile women who fail to show a premenstrual nidatory endometrium a day or two previous to the expected period. These injections are preferably given during the latter half of the menstrual cycle; 2 ampoules of aqueous extract of corpora lutea from pregnant cattle being given daily for 10 days.

Kaufmann, in Germany, reported transforming the atrophic uterine mucosa of castrated women into a secretory functioning premenstrual mucosa by the administration of enormous doses of **theelin** (310,000 mouse units) followed by large doses of **progestin** (corpus luteum factor) totaling 90 rabbit units.

The use of anterior pituitary-like substances (**antuitrin S, follutein, prolan**), however, is even more successful in regularly menstruating women, in stimulating luteinization and creating an endometrium favorable for nidation. This substance, obtained from the urine of pregnant women, is capable

of evoking an ovarian response in the rodent qualitatively identical with that of implants and extracts of anterior lobe tissue. Functional uterine bleeding, if due to pituitary deficiency, responds very favorably to this plan of treatment, but only 10 per cent of amenorrheic women respond to treatment with the product when it is employed as the sole agent.

The relative ineffectiveness of prolan in hypophysectomized animals led to the conclusion that in the normal animal it either stimulates the pituitary sex cells to increased activity or converts an inactive substance (prohormone) in the hypophysis into an active sex hormone. Mazer and Katz report 50 patients with menstrual deficiencies who received thrice weekly injections of 4 c.c. (1 dram) of **pituitary extract** containing **prohormone** and 30 to 40 rat units of **prolan** for a period of 7 to 12 weeks. Nineteen of the entire group of 50 responded to the injections in the form of 6 or more regular menstrual flows. The best results were obtained in definite pituitary deficiencies, 13 of 24 women in this class responding favorably to the treatment.

*Irradiation*—Better results are obtained with low dosage x-ray stimulation of the ovaries and pituitary gland than with any other form of treatment for sterile patients with menstrual derangement. In cases of primary ovarian failure with compensatory hyperfunction of the anterior pituitary gland, irradiation of the pituitary gland, however, is theoretically useless and may probably be harmful.

**TREATMENT OF REPEATED ABORTIONS**—In the treatment of repeated abortions of endocrine origin **corpus luteum injections** 3 times weekly, for the first 5 months, are recommended. In addition, the patient may receive in alternating weeks **desiccated thyroid tissue**,  $1\frac{1}{2}$  grains (0.1 Gm.) daily, and **sodium iodide**, 10 grains (0.6 Gm.) daily, unless otherwise contraindicated.

**SURGICAL TREATMENT**—**Lacerations** of the vaginal wall, if present, should be **corrected**, and the same is true of similar lesions of the cervix. In *acute anteversion of the uterus*, **dilatation** and **curettement**, and occasionally the introduction of an **intrauterine pessary or drain**, may be of some benefit, though it is believed that the latter instrument should be used with reluctance. In the presence of a "*pinhole*" os, **mechanical dilatation of the cervix** and **curettage of the endocervical mucosa** is indicated.

At the sterility clinic of the Department of Obstetrics at Jefferson Medical College a brief history card has been made to facilitate the study and classification of these cases. Chart I is a copy of this record.

For the past 3 years careful endocrine studies have been made of all patients presenting evidence of functional sterility. From Table I it is observed that in a group of 100 women of this type, 37 were encountered who menstruated regularly and 63 irregularly. In the course of study a premenstrual curettage was performed on these 37 regularly menstruating women without anesthesia by using a small curette. Microscopic examination revealed the interesting fact that only 16 women showed a normal premenstrual endometrium with characteristic secretory changes evoked by the corpus luteum hormone (progesterin), while 21 patients had either a hyperplastic, an interval, or an atrophic endometrium. In the latter patients the sterility may be due to the fact that these

women are not giving off ova for fertilization. E. Novak (J. A. M. A. 102: 45; (Feb. 10) 1934) contends that these are instances of menstruation without ovulation, which is so common in monkeys and undoubtedly occurs frequently in women.

CHART I (A)  
JEFFERSON MEDICAL COLLEGE HOSPITAL  
DEPARTMENT OF OBSTETRICS  
*Sterility Clinic*

NAME	ADDRESS	AGE	CASE No.
<i>History</i>			
Chief complaint			
Married	Years	Previous Marriages	
Pregnancies		Contraception	
<i>Past History</i>			
Previous treatment		Operations	
<i>Family History</i>			
Examination of husband			
<i>Present Condition</i>			
Menstrual history			
Weight changes			
Other symptoms		Last period	
<i>Examination</i>	Wt.	Ht.	B.P.
Appearance			
Chest			
Abdomen			
Gynecological			

CHART I (B)  
JEFFERSON MEDICAL COLLEGE HOSPITAL  
DEPARTMENT OF OBSTETRICS  
*Laboratory Studies*

'Urine analysis	Blood count	Wassermann	B M R	I
Estrin of blood (premenstrual)				
Anterior pituitary sex hormone of blood				
Eye-ground and field examination				
Glucose tolerance study				
Study of endocervical secretions	ph	Viscosity	Smear	
Postcoital examination	Hours	Vagina	Cervix	
Tubal patency test				
Gas pressure		Shoulder pain	Pneumoperitoneum	
Insufflation post atropine gr				
Lipiodol and x-ray				
Further insufflations				
<i>Endocrinopathy</i>				
Normal	Pituitary	Thyroid	Ovarian	Unclassified
<i>Treatment</i>				

It is also observed in Table I that only 8 women in this group gave evidence of a demonstrable quantity of female sex hormone in the blood just before an expected period, in contrast to the occurrence of a demonstrable quantity of the hormone in over 90 per cent of regularly menstruating fertile women.

The group of 63 irregularly menstruating women is more easily understood from the standpoint of sterility. So closely linked are these menstrual disturb-



ances to the failure to conceive, that every attempt is made to regulate the periods in this group. Most of these women (38) presented evidence of pituitary hypofunction. A small group, however, of 6 women showed a primary ovarian hypofunction, as evidenced, in addition to the clinical stigmata, by a failure to demonstrate female sex hormone in the blood a day or two before an expected period, combined with a demonstrable quantity of anterior pituitary sex hormone in the blood by the Fluhman method, indicating a hyperactivity of the pituitary gland, in an attempt to compensate for a poorly functioning ovary.

TABLE I  
ANALYSIS OF 100 CASES OF FUNCTIONAL STERILITY

	Cases	Results of Treatment		
		Abortion	Full Term Pregnancy	Failure
I Regularly menstruating sterile women ..	37	2%	5%	30%
Types of endometrium.				
Premenstrual ..	16			
Hyperplastic ..	21			
Interval ..				
Atrophic ..				
F S H in Blood (premenstrual).				
Positive reaction ..	8			
Subthreshold ..	9			
Negative ..	20			
II. Irregularly menstruating sterile women	63	5%	12%	46%
Pituitary hypofunction ..	38			
Ovarian hypofunction ..	6			
Hypothyroidism ..	2			
Hyperthyroidism ..	1			
Unclassified ..	16			
Total	100	7%	17%	76%

Table I is an analysis of 100 cases of functional sterility with the results of treatment, as carried out in the Department of Obstetrics, Jefferson Medical College

Analysis of the results obtained by various forms of therapy, including regulating the diet, hormone therapy, curettage and irradiation, reveals the interesting fact that 17 women subsequently became pregnant and carried to full term, 7 women became pregnant but aborted early, and 76 women did not become pregnant, although many of these women were definitely improved clinically. In the light of the rapid advances being made in the manufacture of potent glandular preparations, a ray of hope may still be held forth to this large group of functionally sterile women.

*Artificial Insemination*—The relationship of a relaxed perineal floor to sterility is discussed in Queries and Minor Notes (J. A. M. A. 102:863 (Mar. 17) 1934). A rectocele or cystocele seldom prevents conception. Even women with a partial prolapse of the uterus can conceive. The loss of seminal fluid does not usually result in sterility because, in most instances, enough semen is deposited on the cervix during ejaculation to permit impregnation. However, when the cervix is not in the line of ejaculation, the loss of semen immediately after coitus

may play a part in sterility. Nevertheless, even in these cases, enough semen remains in the vagina to permit fertilization. As a precaution, however, in cases of sterility when there is a tendency to the loss of semen, the patient should remain in bed for at least  $\frac{1}{2}$  hour after intercourse with her hips elevated on a pillow or stay in the knee-chest or Sims position for 10 or 15 minutes.

Before insemination or even a dilation is resorted to, the contents of the cervical canal should be aspirated immediately after coitus and examined to ascertain whether motile spermatozoa are present in this medium. A Rubin test should be performed to make certain that the Fallopian tubes are patent, even though the patient has had 3 children. Not infrequently, pregnancy follows such a test, even when the tubes are permeable. If, however, no gestation follows such a test, it may be advisable to perform a **dilation** and a **mild curettement**, because conception occasionally occurs after this procedure.

The last resort is artificial insemination. Both husband and wife must be told that attempts to impregnate the woman artificially will most likely have to be carried out many times over a period of months. Even then, there may not be a successful result. The most favorable time to carry out this procedure is the 10 days that occur midway between the first day of one menstrual period and the first day of the next expected menses. The ideal time for conception to take place is at the time of ovulation, which usually occurs about midway between menstrual periods. Since ovulation may occur any time from the tenth to the eighteenth day of the cycle, it is advisable to inseminate 3, 4 or 5 times during these 10 days. The husband should be instructed to wash the penis with soap and water before coitus and the wife should take a sodium bicarbonate or salt-water douche. There are 4 methods of procuring semen: (1) masturbation, (2) coitus interruptus with ejaculation into a small jar, (3) coitus condomatus, and (4) natural coitus followed by aspiration from the vagina. The most aseptic method and the one that is not too obnoxious is to have a small sterilized jar at hand before intercourse. At the time of the orgasm the semen should be ejaculated into this jar. The latter should be immediately brought to the physician's office. The patient is placed in the lithotomy position as for a vaginal examination and the vagina carefully cleansed. The cervix is exposed with a bivalve speculum and the external os is further cleansed. However, it is not advisable to apply any antiseptic, because this may destroy the spermatozoa that are to be injected. The cervix is grasped with a tenaculum, and a uterine cannula is gently inserted into the uterine cavity. The semen in the jar is drawn up into a Luer syringe and 1 or 2 c c. of it deposited in the uterine cavity, very slowly. If the semen is injected too quickly, it will be expelled by uterine contractions. After the injection is performed, the cannula should be removed slowly and the patient should lie quiet on the examining table for about 30 minutes. It is best to examine some of the semen just before each insemination, to make certain that it is satisfactory.

*Cervical Dilatation.*—A series of 18 sterility cases in apparently normal women, with no evidence of glandular dysfunction, is presented by C. H. Birnberg (J. A. M. A. 103:1143 (Oct. 13) 1934). All known methods of treatment had been tried without success. When examined, these patients presented an eccentric external os, a very narrow and deviated cervical canal, and some slight

displacement of the uterus. The external os instead of being located centrally, as is usually noted, was situated eccentrically; either at 11 or 2, as on the face of a clock, and very rarely at 5. The cervical canal was so narrow that difficulty was experienced in passing a fine probe. The course of the canal, instead of being straight, was slightly deviated. The displacement of the uterus, usually very slight, varied. The most common displacement was retroversion.

The treatment in all these cases was identical. A gradual **dilation of the cervix** with Hegar dilators was instituted, until the cervix admitted a number 14 dilator. This procedure usually necessitated a period of 2 months. The early dilation was associated with some degree of pain. The patients presented themselves for dilation once a week. They were advised to use contraceptive measures until treatment was completed. During each dilation, with the dilator still in the uterus, the patient was put in a knee-chest position and the uterus was gently manipulated to correct any displacement.

The successful outcome of these 18 cases suggests that this method be given a trial in otherwise stubborn cases of sterility.

**Iodized Oil**—G. K. F. Schultze (Zentralbl f Gynak. 58: 180 (Jan 20) 1934) believes that in addition to its value in diagnosis, the introduction of **iodized oil** into the uterus and tubes of sterile women also has a therapeutic effect. In 21 cases, or 13 per cent of those in which the x-rays revealed that one or both tubes were passable, a causal connection must be assumed between the filling with iodized oil and the subsequent pregnancy. It is probable that the introduction of the contrast medium presents a sort of fluid probing the cervical canal. Moreover, the dilation of the uterine cavity, effected by the contrast filling, may play a part. The author believes, however, that the therapeutic action of the contrast medium is due primarily to the action on the tubes. Observations seem to indicate that the iodized oil influences the function of the tubes by stimulating the peristaltic action.

**TRICHOMONAS VAGINALIS.**—O. Glassman (J. A. M. A. 102: 1748 (May 26) 1934) notes that although the vaginal secretion *in pregnancy* is normally increased in amount, this condition is found to be associated with a trichomonas vaginalis infection in 10 to 40 per cent of cases. It is suggested that this infection occurs more frequently in the pregnant woman than in the non-pregnant because the increased amount of female sexual hormone in the body increases the growth of this flagellate.

In a series of 309 unselected pregnant patients, *Trichomonas vaginalis* was found in the vaginal secretions in 20.7 per cent. The symptoms were essentially the same as in the nonpregnant, and the diagnosis is easily made by the hanging drop method. There was no increased puerperal morbidity in these cases.

**Diagnosis**—R. E. Ewing and M. LeMome (Surg Gynec Obst. 58: 192 (Feb.) 1934) describe a new method for the diagnosis of *Trichomonas vaginalis* by a routine Gram-stained smear but the diagnosis is not as definite as when the carbol fuchsin stain method is employed. The technic of making carbol fuchsin stains is simple and includes the following steps: (1) smears are made thin; (2) they are fixed in air, not flamed; (3) the slides are covered with carbol fuchsin

(about 20 to 25 drops); (4) 20 drops of distilled water are added and allowed to stand for 3 minutes; (5) the slides are washed with distilled water and dried between filter or blotting papers; (6) examination is made under an oil immersion lens.

Of 90 smears examined, 66 per cent. were found positive and 34 per cent. negative for *Trichomonas vaginalis*, of these 90 smears, the hanging drop examinations were positive in 41 per cent. and negative in 51 per cent. In 8 per cent. of the cases no hanging drop examination was made. Positive findings in hanging drop examinations were shown in only 63 per cent. of the cases with positive smears.

**Treatments.**—The multiplicity of treatments of *Trichomonas vaginalis* in pregnancy indicates that a satisfactory method has not been obtained. All relieve the symptoms, but reinfection is very prone to occur. This may be due to the fact that as yet the life cycle or focus of the parasite is not known. The methods used may be divided into 2 types: (1) those in which douches or tampons are used with various antiseptics, usually preceded by scrubbing of the vagina with tincture of green soap, and (2) the drying or powder treatment.

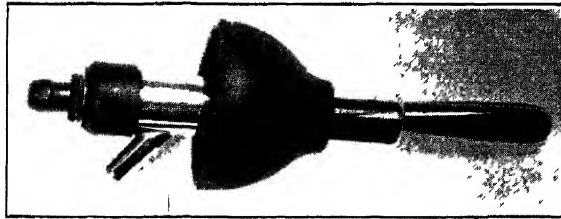
The treatments used in nonpregnant cases, which are rather drastic, are employed in modified form in cases of pregnancy. Hoehne washes the vagina with 1 per cent. **corrosive mercuric chloride** followed by a **glycerin mixture containing sodium bicarbonate or sodium borate**. De Lee favors this method, but advocates putting the patient to bed for 2 days during the treatment. Schmid and Kammiker have used this method with fairly good results. Greenhill, after scrubbing the vulva and vagina with tincture of green soap, uses methylene blue (methylthionine chloride) tamponades followed by 0.5 per cent. lactic acid douches. Mohler injects a solution of Döderlein bacillus culture and lactose into the vagina with a syringe. Hibbert uses a specific streptococcus bouillon filtrate. Cornell and his associates have used mercurochrome, methylene blue, gentian violet, acriflavine hydrochloride, glycerin with and without sodium bicarbonate, tincture of iodine, hexylresorcinol, lead acetate, zinc oxide ointment, metaphen and the like, and they advocate the Kleegman treatment, which consists of scrubbing the vagina with tincture of green soap, painting with pyroligneous acid and insertion of Lassar's paste tampons. Holden uses kaolin as a drying powder. Bland precedes the kaolin with 1 per cent. trinitrophenol and follows with douches of compound solution of iodine. Sure and Bercey use quinine sulphate with insufflation. Northrup advises powdered sulphur, and Gellhorn has obtained good results with acetarsone (stovarsol).

(1) Glassman (*loc. cit.*) has tried a number of these methods which relieved many but were not entirely satisfactory. Lately he has used with very good effect a pure **crystalline phenol** in an acid medium, notably **boric acid powder** instead of the usual sodium bicarbonate, as the sodium bicarbonate often produces an irritation. **Essential oils** are added for their cooling effect. In acute cases the patient is allowed to take daily douches (from 1 to 2 drams—4 to 8 c.c.—to a quart—1000 c.c.—of water) for 1 or 2 weeks, which relieves the symp-

toms and allays the irritation. The vagina is then swabbed with a cotton pledget and the dry powder, mixed with 3 times its volume of boric acid powder, is instilled into the vagina, the patient being instructed to take a douche with warm water the same evening or the next morning. As the phenol content of the douche powder averages from 6 to 8 per cent, it must be mixed with at least 3 times its volume of boric acid powder before it is used dry in the vagina. If used full strength in a sensitive patient, it may cause a severe burn, as did occur in one case.

I. W. Kahn (Am. J Obst and Gynec 28:511 (Oct ) 1934) reports a series of 47 patients in whom prompt relief was experienced by the following technic.

Two quarts of a solution of 2 tablespoonfuls of **sodium perborate** at temperature of 100° F. (37.8° C ) are used to irrigate and distend the vagina, by means of a special occluding vaginal syringe (see Fig.). The fluid is allowed to



Occluding vaginal syringe (I W. Kahn Am J Obst and Gynec.)

run into the vagina through an upper channel in the apparatus, while a tube running from the lower channel carries off the return flow into a bucket. A rubber shoulder on the syringe fits snugly against the vaginal introitus, making it air- and watertight and preventing regurgitation of fluid from the vagina and around the apparatus. The lower tube is pinched off for about a half-minute, thus permitting distention of the vagina and eradicating all crevices, wrinkles, and pockets in the anterior, posterior, and lateral fornices where the trichomonads usually lodge. The pressure on the lower tube is then relaxed and the vagina permitted to empty itself. The maneuvers are repeated until the reservoir is empty. When the fornices are fully distended, the patient usually complains of a fullness or aching in each groin, which denotes maximum stretching of the vault of the vagina and is an additional signal to release the pressure on the lower tube. This distention and irrigation rids the vagina of all inflammatory debris and mucus and cleanses every crevice in the vaginal mucosa and fornices.

After the irrigation has been completed, the vagina is wiped dry, a suitable vaginal speculum inserted, and **quinine sulphate powder** is blown into the anterior, posterior, and lateral fornices down to the vaginal introitus, using a Powdex powder blower. The labia are separated and more powder is blown over the vestibule and external genitals. The patient is instructed to report daily thereafter for 1 week, and every alternate day for the next week. No vaginal douches or suppositories are prescribed. Treatment is not interrupted by a menstrual period, although no irrigations are given during the flow; the vagina is merely wiped dry, freed of clots, and insufflated with the powder.

Sodium perborate was selected as the irrigating agent because it is alkaline and quickly overcomes the hyperacidity produced by the trichomonads. It readily gives off nascent oxygen and is bactericidal to the vaginal flora. The effect of the nascent oxygen is bubbling in character, similar to that of peroxide, and tends to dislodge mucus and debris from the deep recesses of the vagina. Quinine sulphate in experimental tests has proved to be highly destructive to the *Trichomonas vaginalis*. Its continuous presence in the vagina destroys the trichomonads in a very short time and inhibits the growth of spores.

Patients presenting themselves soon after the initial attack responded promptly to the treatment and were found invariably to be free from the trichomonads after the next menstrual period, and remained so thereafter. All the other women who had been suffering from the infection for from 1 to 3 years previously, were cured within from 2 to 4 months, and have been observed for a year or more without treatment.

Only in 2 cases were toxic effects observed from the use of quinine. One patient showed evidences of quinine idiosyncrasy and here the quinine sulphate was mixed with equal parts of starch or zinc oxide powder. In the other case, the patient complained of a menorrhagia probably due to some absorption of quinine from the vagina and its emmenagogue effect upon the uterus. In this case the quinine was similarly treated. The amount of quinine blown into the vagina at each sitting is equivalent to about  $7\frac{1}{2}$  grains (0.5 Gm.) and in very bad cases, no more than 15 grains (1 Gm.). This is enough to coat all the vaginal walls and the external genitals.

**TUBERCULOSIS, GENITAL. — *Diagnosis and Treatment.*** — The value of oxygen pneumoperitoneum in the diagnosis and treatment of tuberculosis of the genitalia, intestine and pneumoperitoneum is discussed by I. F. Stein (Surg Gynec Obst 58:567 (Mar) 1934). In the author's service he has practically eliminated the resort to exploratory laparotomy in pelvic surgery since utilizing diagnostic pneumoperitoneum, and has employed the method in over a thousand cases within the past 10 years.

In suspected pelvic tuberculosis, oxygen is used in place of carbon dioxide because of its therapeutic as well as its diagnostic value in this condition. When tuberculosis is present, often involving the pelvic structures, peritoneum, and intestines, repeated oxygen insufflations are used. No serious accidents were encountered in performing transabdominal puncture. By means of diagnostic pneumoperitoneum, alterations in the size, shape, density, and relationship of the various pelvic organs, and especially the presence or absence of adhesions may be demonstrated clearly in the x-ray film.

It is usually sufficient to insufflate the abdomen with a liter of oxygen to demonstrate the presence of pelvic tuberculosis. The Fallopian tubes in tuberculosis are usually greatly enlarged, tortuous, and thickened so that they cast an unusually dense shadow on the x-ray film, and they are usually patent. Sometimes calcium deposits in the tube wall are demonstrable. Dense intestinal adhesions are commonly found, particularly in the plastic variety, which are readily recognized on the film. A moderate amount of serous exudate is no contraindication.

cation, if large amounts are present, tapping should precede the introduction of oxygen

*Technic*—The procedure is exceedingly simple and differs in no way from that of the transabdominal pneumoperitoneum with carbon dioxide used for gynecological diagnosis. It is advisable that about an hour before treatment the bowels be emptied by means of a **cleansing enema**. One-half hour before, **morphine sulphate** (alone or combined with **scopolamine hydrobromide**) should be administered, the dose depending upon the age, condition, and size of the patient. For the average adult who is in fairly good condition,  $\frac{1}{4}$  grain (0.016 Gm) of morphine may be used, combined with  $\frac{1}{150}$  grain (0.45 mg) of scopolamine. The bladder should be emptied just before treatment. The skin of the lower abdomen is prepared with **alcohol** followed by 2 per cent **mercurochrome solution**, which is allowed to dry. A rather firm, inflexible needle 3 inches in length and fitted with a stylette is introduced through the abdominal wall, no local anesthetic being required. The point of introduction is usually 1 inch to the left of the umbilicus and slightly below that level. The needle is held vertically, between the thumb and third finger, at right angles to the skin, and is introduced into the peritoneal cavity by means of pressure of the forefinger on the stylette. Three resistances are met, first, the skin, second, the aponeurosis, and third, the more sensitive peritoneum. If fluid is present, about a liter may be removed by trochar, and the latter used for insufflation from one-half to the same amount of oxygen being introduced as that of fluid evacuated. A liter of oxygen produces little discomfort from distention and is usually a sufficient dose. The needle is quickly withdrawn and with needle puncture no dressing is required. The patient is kept flat on the x-ray table, the same position being maintained during transportation back to bed, to prevent "shoulder pain" from gas entering the right subdiaphragmatic space. Within 48 hours all signs of oxygen have usually disappeared. Insufflation may be repeated in from 4 days to 2 weeks.

The author cites 64 cases of intraabdominal tuberculosis from the literature and reports 6 additional cases. Two of these represent cures of 4 and 5 years, respectively. In utilizing oxygen therapy, sight must not be lost of the other factors so valuable in the care of the tuberculous patient, *viz*, **rest**, **climate**, **food**, and **tonics** as indicated, and **surgery**, when the condition is complicated by mixed infection. It is evident from some of the case reports cited that intraperitoneal oxygen insufflation is valuable in intestinal tuberculosis and various forms of tuberculous peritonitis if used in the early stages. Terminal infections, moribund patients, or those with advanced pulmonary disease are unsuited for this method.

Whenever tuberculous salpingitis is suspected, it is advisable to utilize oxygen pneumoperitoneum for diagnostic purposes, the films rendering valuable aid in recognizing the pathology, the oxygen at the same time serves a double purpose, being a valuable therapeutic agent. This is readily appreciated by those who employ the method, as the patient shows prompt evidence of improvement. Temperature falls to normal in a few days, pain is less, the patient feels stronger, and begins to gain weight at once. In some instances, a single insufflation is enough, in others, repeated doses may be required, as indicated by the patient's course.

**UTERUS, CARCINOMA OF.—Treatment.**—W. P. Healy (Am J Obst and Gynec 27:1 (Jan) 1934) notes that the conviction is gradually being forced upon the gynecologist that hysterectomy does not give as satisfactory or permanent a cure as formerly believed. Patients with adenocarcinoma of the

corpus in which radiation was used in full dosage, either alone or some weeks before hysterectomy, have remained free from recurrent or metastatic disease and have lived longer than those patients with adenocarcinoma of the corpus treated by hysterectomy before radiation or hysterectomy alone.

In general the plan in all cases has been **diagnostic curettage**, at which time **radium** capsules are placed in the uterus end-to-end in sufficient number to cover the length of the uterine cavity from the internal os to the fundus. The filtration of these capsules is  $\frac{1}{2}$  mm gold, covered with 2 mm. of black rubber, and they contain sufficient radon so that a total dosage of 3000 to 4000 millicurie hours will be given, according to the length of the canal and the number of capsules in 24 to 30 hours. Usually the average dose is about 3600 millicurie hours. The applicator should not be left in the uterus longer than 30 hours, as where long applications of 40 or more hours have been given within the corpus or the cervix, there has been more constitutional and local disturbance than in shorter applications. Within 2 or 3 days following the application of the radium, the **x-ray** cycle may be given. **Hysterectomy**, if planned, is not done for about 6 weeks. Within this plan there has been no operative mortality in the author's series of 134 cases and rarely any undue difficulty in the operations.

*Results of Treatment*—Of the 13 cases of fundal carcinoma admitted to and treated at Jefferson Hospital, B. M. Anspach (Surg Gynec. Obst. 58: 448 (Feb 15) 1934) states that most of these cases were far advanced upon admission. Until recent years **hysterectomy** was the procedure of choice in fundal carcinoma. Four of the cases were subjected to complete hysterectomy, 1 of whom is now alive 8 years after operation; 3 died within a year, 1 lived  $2\frac{1}{2}$  years, and 1 lived for a year, then becoming untraceable.

In 2 other cases of proposed hysterectomy, exploratory section showed widespread metastases, the operation was abandoned and the cases were treated with **x-rays**. Both died within a year.

Seven cases were treated by radiation—5 received intrauterine doses of **radium** varying between 2400 and 7200 mg hours. One received **x-ray** only and was at the same time treated for cancer of the breast. She lived  $3\frac{1}{2}$  years. One case was treated with both forms of radiation. Following primary radium (2400 mg hours), she had **x-ray** in 1926, 3600 mg hours of radium in 1927, 4800 mg hours of radium followed with **x-ray** in 1928. She is now living and well.

The 2 living cases of fundal cancer give an absolute and relative present-day curability of 15.3 per cent. The follow-up represents 92.8 per cent.

The plan of treatment during the past 3 or 4 years has been to have **radium** available at the time of **diagnostic curettage** in all suspected fundal cancer cases, placing it *in situ* immediately. The curettings are examined within 24 hours and the cell type determined. If cancer is present, the radium is allowed to remain for 36 to 48 hours and **subsequent x-ray radiation** soon is made. The subsequent treatment depends upon the clinical factors of age, general condition, obesity, and the cell type.

**CERVICAL CARCINOMA.—Incidence.**—B. F. Schreiner and W. H. Wehr (Surg Gynec. Obst. 59: 616 (Oct) 1934) call attention to the frequency



of malignant disease of the female generative organs at the early age of 30 years or less. These authors report that there were 2405 patients suffering from malignant disease of the female generative organs admitted to the State Institute for the Study of Malignant Disease up to October 1, 1933. They were somewhat astonished to find 114 of these patients were 30 years of age or younger; 4.6 per cent. of the total gynecological malignancies admitted.

Cancer of the cervix uteri in young women constitutes 68 per cent. of the 114 cases presented here, or 4.9 per cent. of the total number of epitheliomas admitted.

Careful inquiry into the histories of these cases revealed (1) that only one of the 78 patients was unmarried; (2) the 77 other patients had from 1 to 8 pregnancies, bearing out the theory that trauma and inflammatory lesions have a large influence in the production of malignancy of the cervix, (3) that all gave a history of discharge, so-called leukorrhea, for varying periods of time up to 7 years; (4) that the important symptoms referable to menstrual periods consisted of bloody, watery, or foul discharge between the regular periods.

Attention is frequently called to the fact that the incidence of cervical cancer is lower in Jewesses. Sorsby says: "The observance of the Mosaic code undoubtedly produces a high degree of sexual cleanliness; and it is suggested that this cleanliness, with its concomitant restrictions on cohabitation at times when rest is probably beneficial, as after parturition and menstruation, is a factor in the lower incidence of uterine cancer among Jewish women—the regulations of the Mosaic code make the appearance of discharges a cause for inquiry as to its nature, and a woman with a blood-stained discharge is theologically 'unclean'." None of the patients in this group were Jewish.

Twenty-three cases of malignancy of the ovary occurred in patients 30 years of age or younger, 6 papillary cystadenocarcinomas, 6 adenocarcinomas, 9 carcinomas, 1 sarcoma, and 1 malignant teratoma.

Malignancy of the ovary occurring in this age period represents 10.6 per cent. of all malignant tumors of the ovary admitted to the Institute. Malignancy of the fundus of the uterus, vagina, and vulva occurs much less frequently.

Cervical cancer in Groups I and II has yielded healings in about the same proportion as the general average in cancer of the cervix, *i. e.*, 50 and 33 per cent. Groups III and IV and V have been only palliative.

One case of epithelioma of the vagina which occurred in a patient 4 months pregnant and which was treated by irradiation, is reported. A normal healthy child was born and there is no recurrence after 14 months.

The authors' only hope of discovering and treating early lesions of the cervix lies in careful gynecological examination bimanually and with a speculum, resorting to biopsy and cauterization in the so-called cervicitis and erosion, to rule out or discover early malignancy.

Cancer of the cervix is curable when treated early. The frequency, according to A. B. Whytock (*Canad. M. A. J.* 30:522 (May) 1934), is 3.5 per cent. of all gynecological cases. The American College of Surgeons reported on 8840 cases of malignancy, with cures for a 5-year period. Of these, 1561 were cases of carcinoma cervicis. Pathologically, 96 per cent. of all cases were squamous-

cell carcinoma, the commonest site being the external os. The internal os acts as a barrier, limiting spread to the uterine body. Spread occurs by permeation of the lymphatic spaces of the peritoneum, thence to the rectum and bladder. Lymphatic node involvement is capricious.

Ninety-seven per cent. of all patients are multiparæ. Chronic irritation is a strong predisposing factor. The lacerated, inflamed and eroded cervix must be regarded of carcinogenic type. Further predisposition is added by the trauma of pessaries, supports and repeated amateurish attempts at abortion. Infrequently, the cervical stump remaining after subtotal hysterectomy is attacked. The symptoms of early carcinoma are not typical, but they are suggestive. Hemorrhage, such as slight spotting after douching, intercourse, or exercise, is the earliest symptom. When to suspect carcinoma is difficult. *Schiller's test* is very helpful. In this test the cervix is painted with Lugol's solution, which stains the normal superficial cells of the cervix containing glycogen a mahogany-brown, while the glycogen-free carcinomatous layer remains unstained. These unstained areas should be examined histologically.

Some measure of *prevention* may be obtained by **repairing every laceration** at the time of labor or soon thereafter; by treating *endocervicitis* either by the application of **antiseptics** or by operations, such as **repair and amputation**, or by **bipolar diathermy**. **Radium** is to be preferred for the *treatment* of early carcinoma. There is not any immediate death-rate and there are many more competent radiotherapeutists than there are surgeons qualified to perform Wertheim's hysterectomy.

**Diagnosis.**—The majority of cervical cancers are not diagnosed until they reach an advanced stage. C. C. Norris (Am. J. Cancer 20:295 (Feb.) 1934) discusses the means available for the diagnosis of early cases, basing his study on 35 extremely early cases.

*Schiller's iodine test* is valuable, but a positive result only indicates that the epithelium is abnormal. Further microscopic examination is necessary to determine whether the lesion is carcinomatous or benign. The test does, however, give information which attracts attention to the most likely spot to examine microscopically.

The use of the *colposcope* is described. It is an instrument used for viewing the cervix, is attached to a bi-valve speculum, and both magnifies and illuminates the surface viewed. Experience is needed for the use of this instrument, but when this is obtained the author claims that alterations in the epithelium undetected by the naked eye are observable, which, when combined with microscopic examination, may lead to the diagnosis of very early cases of carcinoma of the cervix.

In discussing the methods employed for taking sections, the advantages of amputating the cervix over biopsy are advocated in certain cases. If properly performed, preferably with a diathermy-knife, the risk of dissemination is not to be compared with the risk of delay in suspicious cases.

**Treatment.**—IRRADIATION—H. Hofmann (Zentralbl. f. Gynäk. 58: 1886 (Aug. 11) 1934) states that in treatment by irradiation during pregnancy, the greatest danger for the child lies in the possibility of impairment by the rays,

which increases proportionately to the earliness of the pregnancy, because in the earlier stages of pregnancy the distance between the source of the rays and the embryo is still rather small, and even during the second half of pregnancy an impairment by rays cannot be entirely excluded. The danger of damage to the fetus increases with the quantity of rays employed and when a cervical application is made in addition to a vaginal one. The use of x-rays is much more dangerous than the use of radium rays. The mother is in danger because the irradiation may be followed by an abortion and this, in turn, by an infection. Moreover, the author cites a statistical report which proves that the permanent cures are only slightly more than half as frequent after irradiation as after surgical treatment, and he agrees with the statistician that differences in the results of the two methods are sufficiently great to conclude that irradiation is hardly ever justified. He admits, however, that there may be cases in which irradiation must be tried and describes such a case in a woman, aged 27, mother of one child, who asked medical aid on account of a profuse vaginal discharge. It was found that she was pregnant in the fifth month and that an erosion on the cervix was cancerous. Since the woman rejected an operation and insisted on carrying the child to term, irradiation was decided upon. Small doses of radium rays were applied in 2 sessions and x-ray irradiation was entirely dispensed with. The child was delivered spontaneously at the normal time and there were no puerperal complications. The child gave no indication of impairment by rays. Several months after delivery the cervix again showed an erosion, and the woman was again pregnant (second month). The author considers this new pregnancy worthy of note, because pregnancy is rare following irradiation of cervical carcinomas. The woman submitted to a vaginal amputation of the uterus. At present, 2½ years after the radium treatment, both mother and child are doing well. That the subsequent extirpation of the uterus was justified was revealed by the histologic examination of the cervix, disclosing numerous metastases. This also proves the great danger of irradiation with insufficient doses.

*Complications of Irradiation*—The recognition of the possibility of benign stricture of the intestine as a complication following radiation therapy, often months or years later, is stressed by T. E. Jones (J. A. M. A. 103: 1678 (Dec. 1) 1934), for it can very easily be confused with recurrence of a malignant condition. Its detection and surgical treatment may salvage the lives of many patients otherwise regarded as having a hopeless malignant growth. In a series of 520 patients with *cervical carcinomas* having received radiation therapy at the Cleveland Clinic, there have been 7 known cases of benign stricture of the intestine causing obstruction that might easily have been construed as, or confused with, metastatic carcinoma. In 5 of these cases, the obstruction was in a movable segment of the sigmoid and in 2 cases in the small intestine. All these strictures were observed in patients who had been irradiated for carcinoma of the cervix, but the increasing use of radiation for other conditions necessitating exposure of the intestine may result in similar complications. Subsequent to the radiation therapy no evidence of carcinoma was found in these cases and, judging by present-day standards, none of these patients received excessive irradiation.

While x-ray examinations demonstrate lesions in the sigmoid quite readily, strictures in the small intestine are quite difficult to visualize unless the obstruction is practically complete. In this type of case it is inadvisable to give barium in any large amounts, and therefore exploratory operation is warranted, especially in patients in whom there is no evidence of recurring carcinoma in the pelvis.

That x-ray irradiation is not entirely responsible is a justifiable assumption, because patient 5 received no x-ray therapy. Furthermore the lesion in this case was not at the point of maximum intensity, but in the sigmoid several inches away. The causes must then be searched for that contribute to fixation of a certain loop of small or large intestine in the pelvis which is the recipient of the maximum radium and x-ray dosage at that particular point.

In a series of 655 cases of cancer of the cervix under his care at the Woman's Hospital, Ward observed 14 cases in which intestinal complications exclusive of the rectum developed. Thirteen of these presented symptoms of partial or complete obstruction, and one involvement of the sigmoid without obstruction. Some were associated with fecal fistulas. In 8 of these cases the diagnosis was confirmed by operation or autopsy, and in 7 of them metastatic carcinoma of the intestine was found as well as adhesions and inflammatory exudate. Proctitis, as evidenced by diarrhea, rectal pain and ulcerations, has occurred in about 3 per cent. of the cases. There were 22 rectovaginal fistulas with 3 spontaneous and 2 operative closures, and 21 vesicovaginal fistulas with no spontaneous and 2 operative closures. Eighty-eight per cent. of these fistula cases were classed in Groups III and IV on their first visit, and 5 had developed the complication previous to the irradiation. Ward, therefore, believes that the extent of the cancer was the causative factor in the majority of these cases rather than the irradiation. Carcinoma of the cervix stump following a supravaginal hysterectomy occurred in 47 of 655 cases, or about 7 per cent. In these the incidence of fistula was about twice that in old cases. He believes that irradiation under these conditions is much more dangerous, as the bladder lies on top of the cervix at the site of the amputation, where it will come in close contact with the radium tube placed in the cervical canal. Consequently in these cases he has reduced the initial dosage about one-half and repeats as necessary.

Ward has encountered ureter and kidney complications from obstruction in 18 cases as a late result. In many he believes it due to contraction of post-irradiation connective tissue formation in the broad ligaments, and it is now his practice to pass ureteral catheters as a diagnostic measure in all late cases in which pelvic symptoms develop. Severe deep-seated pelvic pain and edema of the extremities may be due to the same cause and not necessarily to metastatic cancer. He is inclined to the belief that prolonged and repeated high voltage x-ray therapy is the most probable cause in the majority of cases of benign stricture of the intestine, as the effective range of the radium is so limited, except in those cases in which a loop of intestine is adherent to the posterior surface of the uterus or cul-de-sac. Ward advocates that in all cases in which late post-irradiation symptoms of intestinal or ureteral obstruction, severe pain or edema develop, an **exploratory laparotomy** be done with the object of making an

exact diagnosis and relieving the obstruction if due to benign adhesions, **enucleation of any involved pelvic glands** and a **sympathectomy of the pre-sacral nerve** for the relief of pain. As many of these patients develop symptoms after the customary 5-year period of observation, he considers that a 10-year period is necessary for the more correct evaluation of radiation therapy.

**RESULTS OF TREATMENT**—B. M. Anspach (Surg Gynec Obst 58:448 (Feb. 15) 1934) discusses the 5-year results in the treatment of the female pelvis at the Jefferson Hospital.

One hundred and fourteen cases of cervical cancer were seen and 104 treated. Of the 114 cases, 14 or 12 per cent., were Class I and II (Schmitz), only 2 cases (17 per cent) falling into Class I; 81 cases, or 71 per cent, were in Class III, 16, or 13.6 per cent., were in Class IV; while 3 cases, or 2.6 per cent. (first treated elsewhere), were in Class V. Of the 114 patients applying for treatment, 20 are now alive and well, a present day absolute curability of 18.4 per cent.

The simple classification of low grade, intermediate, and high grade malignancy is employed. Most of the cured cases were of the intermediate group. Prognosis from cell type alone is of limited value, the outcome depending fully as much upon the duration and extent of the lesion and the resistance of the patient.

While deep **x-ray** therapy cannot be adopted routinely and seems to be of questionable value as an adjuvant to **radium**, especially in earlier cases (Classes I and II), it is certain that the immediate use of radium in widely extended cervical cancer, and especially the infected and sloughing one, should be limited. Here the x-ray primarily is safer and, except in very fat women, very satisfactory, sometimes being all that is required for regression of the growth and a subsidence of symptoms, or at least providing a more favorable field for the radium. It is very desirable to have at hand radon in seeds and in a bomb to use as the occasion requires.

**VAGINA.—Biology.**—The results of investigations on the biology of the vagina, involving a study of glycogen in the vaginal epithelium and of the bacterial flora and secretion of the vagina from infancy to old age are described by R. Cruickshank and A. Sharman (J Obst and Gynec Brit Emp 41:190 (Apr) 1934).

The presence of glycogen, associated with a deep, many-layered epithelium, has been demonstrated in the fetus, in infants up to the third or fourth week of life, and in women during the reproductive period. Glycogen is absent from the vagina of children from one month to puberty, when it reappears and may antedate the onset of menstruation. It is absent or scanty in women following the menopause, whether naturally or artificially produced. Glycogen could not be demonstrated in the vaginal epithelium of lower animals such as cow, sheep and pig.

The correspondence between the presence of glycogen in the vagina and the reproductive period in the human female suggests that the deposition of glycogen in the vaginal epithelium is dependent on ovarian activity. The apparently anomalous finding of glycogen in the vagina of the fetus and newborn child may be

explained by the presence of estrin, which the writers have demonstrated in the urine of infants during the first 3 or 4 days of life and which seems to be derived from the maternal circulation by way of the placenta. Other evidences of ovarian hormone in the infant's circulation are engorgement of the breasts and vaginal hemorrhage: these two phenomena are frequently associated in the female child.

The results of these investigations, therefore, are compatible with the view that the presence of glycogen in the vagina is dependent on a supply of ovarian hormone (estrin) in the circulation.

An extensive series of observations were made by the same investigators on the bacterial flora and secretion of the vagina at all ages, from birth until after the menopause, and also during pregnancy. In the virgin there are 4 alternating phases so far as the biology of the vagina is concerned.

Soon *after birth*, and for the first 2 or 3 weeks of life, a simple homogeneous flora of Gram-positive bacilli, known as Doderlein's vaginal bacillus, is established in the vagina in association with a highly acid nonpurulent secretion.

After the *first month* of life and throughout childhood until puberty, the bacterial flora of the vagina is sparse and varied, while the secretion is scanty or absent and, when measurable, alkaline in reaction.

At *puberty* there is a sudden reversion in the vagina to the type of flora and secretion found in the first week of life. The simple bacterial flora and highly acid secretion apparently persist in the healthy woman until the menopause.

Following the *menopause* there is a return to the sparse flora and scanty alkaline secretion found in the vagina before puberty.

These findings correspond closely with studies on the presence or absence of glycogen in the vaginal epithelium reported. When glycogen is present, as in the newborn infant and during the reproductive period, the homogeneous bacterial flora and highly acid secretion appear. When it is absent, the secretion is scanty and alkaline and the bacterial flora usually varied. Obviously, the glycogen is being utilized with the consequent production of acid which soon reaches such a concentration that only acid-resistant bacteria such as Doderlein's bacillus can survive and multiply. In this way a defense-mechanism is produced in the vaginal cavity capable of preventing the establishment there of foreign and possibly harmful bacteria.

In *pregnancy* the protective mechanism may be absent in the early months and is developed as pregnancy advances. The explanation of this phenomenon is probably associated with the overproduction of estrin which occurs in pregnancy, and which the writers believe is responsible for the deposition of glycogen in the vaginal epithelium.

In a further study by these investigators (*Ibid* 41:369 (June) 1934), a combined clinical and laboratory examination of leukorrhea in the virgin was undertaken as a result of which the condition was divided into 2 categories, *i. e.*, (1) vaginal discharge of noninfective origin, and (2) vaginal discharge of infective origin. It is with the former that the present study is mainly concerned, as it is intimately related to the previously reported investigations on the biology of the vagina.

Vaginal discharge of noninfective origin occurs as a pathological condition in virgins and normally in pregnant women and is due to an excess of the normal vaginal secretion. The discharge itself is white, caseous in consistence, highly acid in reaction, and consists of desquamated vaginal epithelium, lymph and Döderlein's vaginal bacilli. It is thus similar in character to the vaginal secretion of newborn infants and healthy women of the reproductive period. It is suggested that an excess of the estrogenic hormone, by causing increased deposition of glycogen in the vagina, produces the vaginal discharge of noninfective origin described. Excess of estrin occurs normally in pregnancy, particularly in the later stages. In virginal leukorrhea, which is not infective, the authors' data suggest that an excess of estrin may in certain cases result from a disturbance of the normal balance between the anterior pituitary and ovarian hormones.

# PEDIATRICS

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**ANEMIA IN CHILDREN.—ANEMIA OF PREMATUREITY.**—According to K. K. Merritt and L. T. Davidson (Am. J. Dis. Child 47:261 (Feb) 1934), who studied groups of untreated premature and immature infants, the value of the red cell count at birth for normal infants in their series was 5,950,000; that for immature infants, 5,810,000; and that for premature infants, 5,540,000. The erythrocytes fell more rapidly through the first few months in the premature and immature groups than in the normal. At the second month their values were, for the normal, 4,740,000; for the premature, 3,910,000; and for the immature, 4,040,000. The erythrocytes of the full term infants remained thereafter at about 4,610,000 and those of the immature infants at 4,020,000 or above, whereas those of the premature infants from the second to the seventh month remained consistently below 4,000,000.

Hemoglobin value for the normal infant at birth was 23.4 Gm.; the immature, 23 Gm.; and the premature, 21.65 Gm. At the second month the normal was 13.1 Gm.; the immature, 11.8 Gm.; and the premature, 11.0 Gm. At 1 year the normal figure was 12.4 Gm.; the immature, 10.8 Gm.; and the premature, 10.3 Gm. (at 10 months).

It has been shown that the amount of iron of the premature infant is very little lower than that of the normal infant, but, as growth is more rapid, the reserve of iron becomes depleted more rapidly. The physiologic drop of the blood seen in the normal infant is exaggerated in the premature infant and occurs probably coincidentally with the depletion of the store of iron. There is probably an added factor in the instability of the hematopoietic system, an instability which it shares with the circulatory and gastrointestinal system. The lowered function prevents a sufficiently rapid regeneration of the blood, unless therapy is resorted to.

**Treatment.**—Two groups of premature infants were treated with **iron and iron and raw liver** in combination in an attempt to prevent anemia. Iron was given chiefly in the form of **iron and ammonium citrate** (50 per cent aqueous solution). A few patients received **albuminized iron**. The dosage of iron and ammonium citrate was 0.3 Gm. (5 grains) per kilogram (2 $\frac{1}{2}$  pounds) a day, or 0.05 Gm. ( $\frac{5}{8}$  grain) of reduced iron per kilogram. Albuminized iron was used in a dosage of 0.3 Gm. (5 grains) per kilogram a day. Iron when given alone was started at from the seventh to the tenth day of life. Iron and liver when given in combination was started at from the seventh to the fourteenth day. The liver was usually started a few days after the iron, and was given in doses of 5 Gm. (1 $\frac{1}{4}$  drams) per kilogram. Comparing these two groups, the lowest level of the red cell count was approximately the same at 3,900,000, while both groups rose rapidly to cross the 5,000,000 mark at the fifth to the sixth months. The group receiving iron alone reached a slightly higher level at the sixth month than did those receiving iron and liver.

Another group of prematures was studied in whom therapy was not started until after they became anemic. At the second month the red cell count had fallen to approximately 3,190,000 and the high level was reached at the tenth month.

This would seem to indicate that recovery in infants who receive no treatment before the erythrocytes reach the lowest point is considerably delayed.

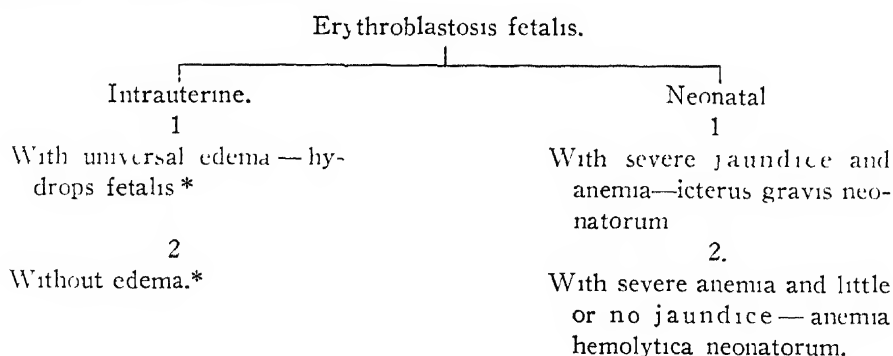
The advantage of liver and iron in combination, as compared with iron alone, seems negligible in its effect on the hemoglobin. Both groups reached a low level at the second month, approximately 11 Gm., and at the eighth month rose to about 14 Gm. In the group treated after anemia had developed the hemoglobin fell at the third month to 9.2 Gm., and rose to 13 Gm. at 1 year.

The authors feel that though the initial drop in both erythrocytes and hemoglobin could not be prevented altogether, it was less marked in the infants who received early therapy, and the upward trend began earlier in the treated patients (2 months instead of 3) and was maintained at a higher level throughout the first year.

The authors recommend that **iron** as well as the **antirachitic vitamins** and **orange juice** should be given as a routine to all *premature infants* of from 2 to 3 weeks of age and continued until they have attained 6 months of age or until the blood has reached a normal level. Prophylactic treatment since this work was begun has obviated the necessity of therapeutic transfusion in the premature infant.

**ANEMIA OF THE NEWBORN** (*Hemolytic Anemia of Newborn; Congenital Primary or Idiopathic Anemia*)—According to J. C. Hawksley and R. Lightwood (*Quart. J. Med.* 3: 155 (Apr.) 1934), anemia of the newborn is closely related to 2 other conditions of the newborn, *viz.*, icterus gravis neonatorum and hydrops fetalis. All three of these diseases show the presence of nucleated red blood cells, chiefly erythroblasts and normoblasts, in the peripheral blood stream in excess of the physiological maximum for the age. The authors group these three clinical entities under the term erythroblastosis fetalis. Icterus gravis is usually a clearly defined disease, often familial and showing a tendency for the first-born to escape. Subsequent infants may be stillborn or affected with icterus gravis, hydrops fetalis or anemia gravis, or a combination of conditions may be seen in the same infant.

Diagrammatically expressed as,



Thus, erythroblastosis fetalis may comprise 3 different clinical syndromes which may overlap and the same mother may have successive children presenting in turn these different manifestations.

\* Often stillborn

Rautman called the extramedullary hematopoiesis—erythroblastosis. Schridde, in 1910, noted similar pathological changes in hydrops fetalis and the hemolytic anemia of the newborn. The appearance of numerous immature red cells in the peripheral blood has been called erythroblastemia.

According to R. Lightwood and J. C. Hawksley (Proc. Roy. Soc. Med. 27:255 (Jan.) 1934), blood features of the condition are: a severe hemolysis, and evidence of considerable regenerative activity, which is shown by an outpouring of newly produced immature red blood cells,—megaloblasts, normoblasts, and reticulocytes together with a smaller number of immature white blood cells. In infants that do not die this response results, after the cessation of the hemolysis, in a return of the blood to normal.

**Pathology.**—At the height of the jaundice and the severest anemia, foci of blood-forming tissue, principally erythropoietic but partly myelopoietic, are found in most organs, chiefly the liver. Besides this, there are toxic changes and necrosis in the liver cells with a deposition of bile pigment and iron; kern-ikterus or staining of the basal nuclei, a pathological condition, named by Orth, who first described it in 1875. This cerebral staining, which also affects the nuclei in the medulla, is responsible for certain of the deaths occurring within the first 5 days and is the cause of residual extrapyramidal symptoms at a later age period (spasticity, athetosis, mental defect). The authors have noted the correlation between hepatic and extrapyramidal cerebral lesions in erythroblastosis fetalis and this may throw light on the relationship between progressive lenticular degeneration and kern-ikterus.

**Symptomatology.**—The disease is familial in nature. Pregnancies are usually normal. The placenta may be enlarged to about double its normal bulk, liquor amnii may be yellow and the vernix caseosa golden in color. Jaundice may be present at birth, or during the first 48 hours or later. The color may be noticed in the face, spreading later to the trunk and limbs.

Conjunctivæ are usually affected. The icterus is mainly hemolytic in character with urobilinuria and a positive indirect van den Bergh in the serum. The depth of the jaundice may vary in response to periods of increased blood destruction. The icterus may disappear in 2 or 3 weeks or may persist for 2 months or more. Other symptoms are a hyperchromic anemia, drowsiness, hemorrhagic tendencies, enlargement of the liver and spleen, presence of fever and nervous manifestations.

**Diagnosis.**—The presence of golden yellow vernix caseosa should always arouse suspicion. The presence of splenomegaly and hepatomegaly should be established and urine and stools examined for bile pigments. Congenital syphilis should be excluded by the Wassermann test and by radiography; acholuric jaundice, by the fragility test. Simple physiological jaundice should be differentiated. This condition arises on the third day, later than icterus gravis, and is neither so severe nor so prolonged. There is no anemia and no erythroblastemia. In cases of congenital obliteration of bile ducts the jaundice appears later and lasts until death occurs. It is always fatal. Anemia occurs later and erythroblasts are not found. The blood picture and splenomegaly will serve to rule out melena neonatorum and intracranial trauma.

**Prognosis.**—The mortality rate of icterus gravis is high; that of hemolytic anemia is low. Rapidly developing jaundice and severe anemia are bad signs. Hemorrhages from the umbilicus or from the mucosæ are of grave significance and often result in death. Medullary failure is to be feared in the first 5 days. Repeated convulsions are serious and may indicate intracranial hemorrhage or kern-ikterus, perhaps with subsequent mental change and spastic conditions of the limbs. Arrest of hemolysis with steadying of the red cell count and diminution of bilirubinemia and improvement in the blood picture is a good sign, but further hemolysis may occur.

**Treatment.**—Lightwood and Hawksley have used repeated transfusions of whole blood and achieved satisfactory results even in some of the most severe cases. As an indication for transfusions the red blood cell level is watched. Any infant with much less than 4 million red cells is transfused at intervals of 4 to 7 days until the count is maintained at or above that level. Transfusions have varied from 40 to 120 c.c. in volume and from 1 to 4 in number. Rapid hemolysis may continue even after transfusion, showing that transfused blood acts by substitution and not by supplying any hypothetical antihemolytic substance. D. P. Arnold and R. A. Downey (New York State J. Med. 34: 579 (July) 1934) watch the hemoglobin carefully in all suspected cases and give intravenous transfusions for 3 or 4 days. An **intravenous drip** can be used for administering fluids. Breast-fed infants should be kept at the breast. **Glucose** is given by mouth for its protective action on the liver.

**NUTRITIONAL ANEMIA.**—According to L. Parsons and J. C. Hawksley (Arch. Dis. Child. 8: 117, 1933), nutritional anemia can be divided into 3 age groups: (1) congenital nutritional anemia, (2) nutritional anemia of early infancy, and (3) nutritional anemia of later infancy and early childhood.

In the congenital variety the most striking symptom is pallor, which is usually marked from birth or develops shortly afterward. This type must be differentiated from the hemolytic anemia of the newborn.

In the nutritional anemia of early infancy the pallor begins at or about the fourth month and it is probable that there is a combined prenatal and postnatal deficiency. The incidence of this variety is higher in twins than in single pregnancies.

The nutritional anemia of later infancy and early childhood is not noticed until about the seventh month. The history of these patients shows that they have been fed on cows' milk or artificial food, occasionally that they have been kept on breast-milk past the proper weaning period or that the child has suffered from some severe infection.

**Etiology.**—The diets taken by the mothers of infants suffering from congenital nutritional anemia are not infrequently very inadequate and the mothers themselves may exhibit hypochromic anemia. Their obstetric histories may reveal the occurrence of stillbirths or of weakly babies. Parsons and Hawksley believe that an adequate diet for the mother can prevent this condition. A. V. Neale and J. C. Hawksley (*Ibid.* 8: 227 (Aug.) 1933) agree that anemias in pregnancy may have far-reaching effects upon the fetus *in utero*. Clinical observations which they made show that nutritional anemia may show itself in the new-

born child, or become apparent during the milk-feeding period. In their opinion, there appears little doubt that a congenital anemia may be a true nutritional anemia, and that it may be due to deficiency in the maternal diet. The transference of hemopoietic substances from the mother to the fetus is progressive throughout pregnancy, and considerably increased in the later weeks. This transference of iron and its allied hemopoietic substances occurs in order to make provision for fetal hemopoiesis and to accumulate a store (principally in the liver) which will be available during the milk-feeding period of early life. It is recognized that such fetal storage principally occurs in the latter weeks of the normal full-term pregnancy. Neale and Hawksley believe that if the total available quantity of iron in the maternal tissues is insufficient, there will be a deficiency of these substances in the fetus, and a simple anemia may be expected at birth or shortly afterward. M. B. Strauss and W. B. Castle (*Am. J. Med. Sc.* 185: 539, 1933), however, contend that anemia of the mother does not produce anemia in the child.

**Symptomatology.**—The blood picture shows an anemia of the hypochromic microcytic type. The less severe anemias show a fall in the hemoglobin, with little if any diminution in the red cell count, while in the more severe anemias the hemoglobin values are still lower, with a smaller drop in the red cell count. Reticulocytes are either absent or very low in number. Occasional normoblasts are found in the more severe cases. The fragility of the red cells is normal. Platelet counts are normal also. Intercurrent infection may cause some change in the blood picture and immature forms of white cells may be seen on such occasions. The spleen may be palpable, but enlargement of the lymphatic glands is absent. The general nutrition of the baby may be good.

**Treatment.**—*Iron Therapy*—L. G. Parsons and J. C. Hawksley (*loc. cit.*) used a preparation of reduced iron in doses of  $\frac{1}{2}$  to 1 grain (0.03 to 0.6 Gm.) 3 times a day. The effects of adding iron to a child with nutritional anemia due to iron deficiency are as follows: A reticulocytosis; a fairly rapid rise of erythrocytes to normal or slightly above normal; a gradual rise of hemoglobin to normal; and, finally, a reduction in the number of red cells to normal directly after the final stages of the hemoglobin rise. John Cason (*J. Pediat.* 4: 614 (May) 1934) uses 5 to 10 c.c. ( $1\frac{1}{4}$  to  $2\frac{1}{2}$  drams), according to the ages, of a solution containing 0.5 Gm. ( $7\frac{1}{2}$  grains) of **cupric sulphate** and 10 Gm. ( $2\frac{1}{2}$  drams) of **ferric ammonium citrate** per 100 c.c. ( $3\frac{1}{3}$  ounces) of 25 per cent **aromatic elixir solution** (U. S. P.). In this way each patient receives daily 10 to 20 mg. ( $\frac{1}{6}$  to  $\frac{1}{3}$  gram) of copper and from 250 to 500 mg. (4 to 8 grains) of iron. This makes a palatable and inexpensive mixture. S. Maurer, J. Greengard, W. L. Curtis and C. K. Kluver (*Ibid.* 4: 356 (Mar.) 1934) studied a group of 12 artificially fed infants and found negative iron balances, the more severe anemias being present in the group with a high negative balance. They also found that a small quantity of **breast milk** facilitated the absorption of iron from the gastrointestinal tract. In their artificially fed infants copper and iron showed no more effect on the iron balance than iron alone. **Liver extract and iron** produced the most marked improvement in the iron balance of the infants studied, whether the iron was derived from inorganic salts or from hemoglobin. E. Gorter (*Am. J.*

Dis Child. 46. 1066 (Nov.) 1933) emphasizes that in the treatment of nutritional anemia it is advisable to **reduce the amount of cows' milk** and **increase the vegetable and fruit** content of the diet. C. A. Elvehjem, E. B. Hart and W. C. Sherman (*Ibid.* 4: 65 (Jan.) 1934) tested the hemoglobin-forming properties of various milk cereal diets on rats and found that the daily addition of 3 Gm. (45 grains) of any of these cereals to the milk diet failed to induce hemoglobin formation, and that the addition of iron to the cereals accomplished hemoglobin regeneration almost comparable to that obtained with mineralized milk. The addition of iron and copper to the cereal products produced better appearing animals, although the hemoglobin formation was little improved over the addition of iron alone. M. C. Lottrup (Am. J. Dis Child. 47: 1 (Jan.) 1934) studied the effect of ferrous and ferric compounds, reduced iron and a copper compound on anemia in children. He concludes that ferrous salts cause a quick and considerable rise in the hemoglobin percentage, while ferric preparations seem to be without effect. The addition of cupric sulphate also seems to be without effect. Ferrous compounds do not cause gastric symptoms, as do reduced iron compounds. M. O. Schultze and C. A. Elvehjem (J. Biol. Chem. 102. 357 (Oct.) 1933) found that neither iron nor copper alone can produce a typical reticulocyte response in rats suffering from severe nutritional anemia. Iron alone fails to initiate a response, while copper alone produces a small prolonged response. The results with copper alone are undoubtedly due to the action of the copper on small available supplies of iron in the body. When these anemic rats were given both iron and copper, a marked reticulocytosis was noted, together with an increase in hemoglobin and red cells.

**Erythroblastic Anemia of Childhood** (*Erythroblastic Anemia of Childhood* (Cooley); *Cooley's Anemia*) —R. Crawford and Richard Williamson (Am J. Dis. Child. 46. 565 (Sept.) 1933) report another case having typical findings of an erythroblastic anemia. The child had a definite mongoloid facies. The blood picture showed overstimulation of the bone-marrow, constant leukocytosis, many nucleated red cells, and an absence of fragility of erythrocytes. The x-rays showed a thickening of the cranial bones. Early changes in these bones revealed a mottled spongy marrow; later, vertical striations appeared. The long bones showed a thin, transparent cortex and an abnormal amount of reticulation in the medullary portion. The ilæ and scapulæ had fan-like striations. In this case a **splenectomy** was performed. Nearly 6 years later the child was growing normally.

David Parker (New England J. Med. 208. 1147 (June) 1933) reports another typical case of this disease in a 6-year-old boy. J. M. Baty, in discussing the case, states that the disease is thought of as being primarily a disturbance of hematopoiesis, primarily involving the bone-marrow. He believes that the x-ray changes are simply secondary to a hyperplastic, actively growing marrow in a young individual whose bones are not entirely fixed. The rôle played by the spleen in controlling the outflow of cells from the bone-marrow into the circulation is not known. After splenectomy in any individual there is a transient rise in young red cells, in the leukocytes, and in the platelets, with a rapid return to

normal within about 2 weeks. Baty believes that splenectomy is contraindicated in erythroblastic anemia because of the danger of spontaneous thrombosis.

**Erythrocytic Fragmentation.**—T. B. Cooley and P. Lee (J. Pediat. 3:55 (July) 1933) describe a process of blood destruction known as erythrocytic fragmentation, seen in erythroblastic anemia and in some of the secondary anemias. This phenomenon is best observed in the moist sealed preparations kept in the warm box at 32° to 37° C., and is usually accompanied by signs of marrow hypoplasia, as shown by lack of regenerative forms. In fragmentation the red cells develop into poikilocytes, then by vibration break off fragments of various sizes and shapes. The authors studied 3 cases of erythroblastic anemia, all of whom had their spleens removed. The increased pigmentation of the serum indicated abnormal destruction, which was attributed to hemolysis in spite of increased resistance to hypotonic solutions, until the moist films were studied. These showed extreme fragmentation even when the hemoglobin and the red cell levels were practically stationary. The balance was due to the great increase in erythropoiesis. The fragmenting cells showed all the forms which have been previously described. Cooley believes that most, if not all, of the microcytes seen in the blood of patients with hypochromic hypochlorhydric anemia are produced by this method and that these are not produced in the marrow. In 2 cases of hemolytic icterus there was no indication of fragmentation, and the microcytes, which are an important characteristic, are probably formed as such in the marrow and are not the result of division in the blood stream. Poikilocytosis, which they believe to be evidence of fragmentation, is not, in their experience, met with in hemolytic icterus, although it has been noted in case reports. Both means of destruction might be at work and explain the occasional failure of splenectomy.

The *blood picture* of erythroblastic anemia has been described by K. Kato and H. Downey (Folia hæmat. 50:55, 1933) as showing the presence of a comparatively large number of very immature normoblasts in the circulating blood. Erythropoiesis may be seen in all its stages. The irregularity in the distribution of hemoglobin within the mature red cells, the extreme degree of anisocytosis, and the moderate amount of polychromasia with very slight tendency to poikilocytosis are the general characteristics of the red blood cells. The authors state that whenever there appear a large number of very immature erythroblasts in the circulating blood, Cooley's erythroblastic anemia may be suspected. The final diagnosis will be reached when this blood picture is correlated with the findings of clinical and x-ray examinations.

**HEMOLYTIC ICTERUS IN CHILDHOOD.**—*Diagnosis.*—M. Grob (Jahrb. f. Kinderh. 142:163 (Mar.) 1934) points out that the diagnosis of hemolytic icterus in childhood may offer difficulties particularly during the crises. The sudden onset of the hemolysis, which leads to a crisis, not only causes an aggravation of the symptoms already present, such as the icterus, anemia, and enlargement of the spleen, but also the appearance of a number of new symptoms which make the symptomatology of the crises extremely varied.

A differentiation may be made according to the predominance of the one or the other symptom. The thermic crises are characterized by increases of temperature that frequently persist for long periods. During the crisis-free intervals



the rectal temperatures are often considerably increased, while the axillary temperatures are normal. The abdominal crises may suggest acute appendicitis. The hemolytic crises frequently lead to severe anemia and to severe reactions of the bone-marrow, with elimination of young red cells and of white cells, so that the blood picture resembles that of leukemia.

**APPENDICITIS IN CHILDREN.**—*Diagnosis.*—C. J. Baumgartner (Arch. Pediat. 50: 571 (Aug.) 1933) has reviewed 100 consecutive records of children who were operated on for appendicitis. He was particularly impressed by the high percentage (55) of ruptured appendices, more than one-half of which were in children under 5 years of age. He notes that perforation, in large measure, is due to delay in diagnosis and hence delay in operation. The danger of depending on the history or the child's complaint is apparent from the fact that only 69 per cent of the children with acute appendicitis and 76 per cent. of those with ruptured appendices complained of general abdominal pain, and only 19 per cent of the acute nonperforated cases and 12 per cent of the children with perforated appendices localized their pain to the right side. Tenderness in the right lower quadrant was the most constant finding in this series. It occurred in 94 per cent of the acute and in 80 per cent of the chronic cases. Intercurrent respiratory infections were frequently encountered. The author emphasizes the fact that observation of the child's breathing may be an aid in differentiating between a pulmonary infection and an acute abdominal infection. The abdominal muscles are splinted when an acute infection is present within the abdomen, whereas, this is not so likely in the case of a respiratory infection.

*Complications.*—A case of bilateral hydrosalpinx secondary to a chronically perforating appendicitis in a 12-year-old girl is reported by A. T. Walker (Am. J. Obst. and Gynec. 26: 448 (Sept.) 1933). During the 2 years before the author saw this patient, she had had 6 attacks characterized by pain in the epigastrium, nausea and vomiting which was followed by localized pain in the right lower quadrant. She was seen by the author at the time of her seventh attack.

In addition to the above symptoms, she had fever and one week before had had a thin bloody vaginal discharge for 3 days, which recurred again the day before examination. Operation disclosed a perforated appendix and bilaterally enlarged Fallopian tubes which contained a fluid identical with that of the previous vaginal discharge. It was the author's opinion that the appendix had ruptured previously during one or more of the attacks and that the perisalpingitis was a result of such an infection. Because these attacks had been attributed to pains associated with beginning menstrual activity, the author warns against the danger of this practice without careful examination and study of the individual case.

**CHICKENPOX (VARICELLA).**—The occurrence of chickenpox in patients at the extreme ages of life is of interest because of its rarity. A typical chickenpox eruption was observed recently in an infant 8 days old, by W. B. Henderson (J. Pediat. 4: 668 (May) 1934). The mother had had a few red papules on the thigh at the time of delivery. This was the only evidence of the

disease in the mother, and was of such little consequence that she failed to mention it to her physician at the time. She had been exposed 10 days previously to chickenpox of one of her other children who, in turn, had been exposed 10 days before to a neighbor child with the infection. It was thought that the mother had transmitted the disease to her infant while it was *in utero*.

**Diagnosis.**—One of the early signs of chickenpox noted by O. Lade (Munchen. med. Wchnschr. 80:1215 (Aug. 4) 1933) was a mild diarrhea of thin stools which occurred about 2 weeks before the eruption of the disease. In his opinion, this symptom expresses the stage of beginning invasion of the virus and it was thought possible that the gastroenteric tract was the site of the original infection.

**Immunization.**—Protection against chickenpox is only essential for children in institutions, especially for those who are suffering from other acute infections. Active immunization against this disease was attempted in 13 children by Z. von Gulácsy (Arch. f. Kinderh. 100 75 (Sept. 29) 1933). Intracutaneous injections were made with vesicular fluid obtained from active chickenpox lesions and diluted with 9 parts of normal saline solution. Only 13 per cent of the group of inoculated children who had been exposed contracted the disease and these attacks were abortive forms. Four untreated children who had been exposed developed the infection. The local reactions to the immunizing treatment consisted of redness and slight infiltration which were thought to be due mostly to mechanical irritation. The degree of immunity conferred was not thought to be dependent on the local reaction.

**Complications.**—Considering the high incidence of chickenpox, complications of the disease are extremely rare. Like other so-called "virus diseases," chickenpox has been followed by *encephalitis* in a few instances. An unusual case of encephalitis with a severe form of bilateral *choked disc* and *hydrocephalus* following chickenpox was reported by E. Mayerhofer and J. Breitenfeld (*Ibid* 100 155 (Sept. 29) 1933). The patient was a boy 14 years of age and the symptoms of the complication began 19 days after the onset of the chickenpox. Repeated drainage of the cerebrospinal fluid gave no relief but after a Forster operation (an opening in the corpus callosum), the condition gradually improved and the patient recovered entirely. It was the authors' opinion that the chickenpox encephalitis was an allergic manifestation.

Several patients with *encephalitis* following chickenpox have been observed recently by A. Eckstein (Acta pædiat. 16 606, 1933). All of these children made complete recoveries. He believed that the improvement of knowledge concerning encephalitis has led to a more frequent diagnosis of this condition.

An extensive *gangrene of the skin* developed during an attack of chickenpox in a patient observed by T. M. Watson (J. A. M. A. 102 2179 (June 30) 1934). The boy, who was 6 years of age, had a subcutaneous hemorrhage in the area of a chickenpox vesicle on the fourth day of his illness. This area increased in size and resulted in a large slough of the entire thickness of the skin. Several **blood transfusions** and large amounts of **parenteral fluid** were administered during the acute stage of the disease with beneficial results and the area of the slough was covered with **pinch grafts**.

A superficial *gangrenous area* on the abdomen which developed in a girl, 11 years of age, in the region of an infected chickenpox vesicle, was described by T. R. Nichols (Canad. M. A. J. 30:297 (Mar ) 1934). Purulent material under the crust of the lesion contained staphylococci. The gangrenous area spread through the superficial layers of the skin and caused the death of the patient several days later.

A condition of *aleukia hemorrhagica* developed in a patient of N. Fiessinger, F. P. Merklen and G. Brouet (Bull et mém. Soc méd d hôp de Paris 50:98 (Feb 5) 1934) about 8 days after the onset of an attack of chickenpox. The patient who was a young man, 18 years of age, contracted an ordinary attack of chickenpox from which he was recovering normally, until on the eighth day, purpuric spots appeared in the skin and in the mucous membranes. He rapidly became anemic, the white cells and especially the granulocytes, fell below normal numbers and the bleeding and clotting times became prolonged. In spite of vigorous treatment, the patient died 20 days later.

**Relation to Herpes Zoster.**—Certain similarities between chickenpox and herpes zoster have suggested a common etiologic agent. Opposition to this contention has arisen from many clinicians. The striking differences between the two diseases, according to J. Comby (Bull Soc de pédiat de Paris 8:380 (Oct ) 1933), are the highly contagious character of chickenpox, the ease with which it can be transmitted by inoculation, and the immunity it confers, all of which are properties not possessed by herpes zoster. Other factors which the author believed to indicate a difference in the two diseases were reports of the same disease occurring simultaneously in the same patient, the finding of a cellular increase in the cerebrospinal fluid of herpes zoster patients only, and the occurrence of encephalitis as a complication of chickenpox only. Previous reports of similarity in the complement fixation reactions of the two diseases were found to have been refuted by another investigator employing a similar technic.

More case reports which suggest the transmission of one of these diseases by exposure to the other have been reported recently. C. Gyllensward (Acta Pediat 14:584 (July) 1933) observed an instance of herpes zoster in a man which was followed in 3 or 4 weeks by chickenpox in his son and 14 days later by chickenpox in the 2 sisters of the boy. In a second instance, a small girl developed chickenpox 17 days after exposure to an elderly woman of the family who had herpes zoster. H. S. Davidson (M. Rec 139:410 (Apr 18) 1934) described a typical case of herpes zoster which developed in a man 73 years of age. Three days later he had a generalized chickenpox eruption. The patient's wife had had herpes 6 months previously. An instance of chickenpox resulting from exposure to herpes was reported by K. Schraube (Munchen med Wchnschr. 80:1438 (Sept ) 1933). A patient of his developed herpes zoster at the age of 72 years. The daughter, 52 years of age, who had taken care of this patient, contracted chickenpox 19 days later.

Vesicular eruptions resembling herpes zoster sometimes occur in patients with leukemia. Only one report of chickenpox in such a patient was found in the medical literature, by A. Philadelphia and L. Haslhofer (Arch. f. Dermat. u. Syph. 169:512, 1934). They added another instance in which a chickenpox

infection of a gangrenous nature developed in a patient 51 years of age who had a leukemic lymphadenosis. The distribution of the eruption was not that of a zoster and the diagnosis of the varicella was confirmed by histologic examination of the lesions. The question was raised whether vesicular eruptions in general are typical of leukemia or whether there is a relationship between leukemia, herpes and varicella.

Animal experiments with the virus obtained from lesions of chickenpox and herpes zoster were made by A. Eckstein (*loc. cit.*). The fluid obtained from zoster lesions was injected intracerebrally into apes to produce an encephalitis resembling that observed in human patients. With vesicular fluid of chickenpox vesicles, no such lesions could be produced. It was thought that the herpes zoster virus might be a neurotropic variation of the chickenpox virus. The fact that chickenpox virus occasionally exhibits neurotropic tendencies in producing encephalitis in human patients, suggests that it bears a relationship to the herpes zoster virus.

**CHOREA.—Treatment.**—The treatment of chorea with **typhoid-paratyphoid vaccine** was reported recently by L. P. Sutton and K. G. Dodge (J. Pediat. 3:813 (Dec.) 1933). In 150 children with the disease, the average duration of the attacks was considerably reduced. Unless the patients developed temperatures of 104° F. (40° C) or more, the therapy was found to have but little value. Good results with typhoid-paratyphoid vaccine therapy were also obtained by A. Capper and E. L. Bauer (Am. J. M. Sc. 186:390 (Sept.) 1933). Their series included 23 patients with chorea, 9 of whom had chronic forms of the disease. All but one responded favorably within a short time and especially notable were the results in chronic patients who had suffered from the disease for an average of 4½ months. No unfavorable reactions occurred. Eleven patients were observed 3 to 15 months after the treatment and 7 or 8 were still free from choreiform movements.

In England, certain precautions in regard to this form of therapy were advised by J. Y. Cheetham (Brit. M. J. 2:815 (Nov. 4) 1933). He employed typhoid vaccine in the treatment of 4 children with chorea. The vaccine was administered intravenously over a period of 7 to 10 days. The initial dose was 0.1 c.c. of a vaccine containing in each cubic centimeter 1000 million B. typhosus and 750 million each of B. paratyphosus A and B. The dosage was doubled each day until the patient developed a temperature of 103° to 106° F. (39.4° to 41.1° C). In 2 patients, the course of the chorea seemed to be cut short, in the third there was very little benefit noticed, and in the last patient there was an exacerbation of the cardiac lesion which the author suspected had been caused by the hyperpyrexia treatment. It was the conclusion of the writer that false security might be obtained from such treatment and proper rest for the cardiac condition would not be carried out.

Similar conclusions were reached by H. Fish (*Ibid.* 2:816 (Nov. 4) 1933) from the results of the treatment of 1 patient with **triple typhoid vaccine**. The therapy seemed to hasten the recovery of the child from the choreiform movements but the author was unwilling to believe that the period of rest for

the treatment of the carditis should be shortened in proportion. He advised that the treatment be given only to such patients who had little or no cardiac involvement and to those who had had persistent chorea or chronic relapses.

**Nirvanol** was administered to 55 children with chorea by S. W. Marick (J. Pediat. 4 242 (Feb.) 1934) and no unfavorable reactions were observed. The drug was effective in checking the choreiform movements. About 62 per cent of the group developed rashes, but some of the children with no skin reaction also showed improvement. In an attempt to investigate the subsequent history of patients previously treated with nirvanol, the author found a large percentage had had recurrences of chorea and many had symptoms of cardiac involvement, so that he concluded that the therapy was beneficial in checking moderately severe or severe chorea attacks, but that recurrences could not be prevented.

A comparative study of the value of **typhoid vaccine** and phenylethylhydantoin (**nirvanol**) in the treatment of 47 chorea patients was made by J. A. Monfort (Am. J. Dis. Child 47 1269 (June) 1934). Of the group of 24 who received phenylethylhydantoin, 8 were unimproved and 1 died. There were 23 who were given typhoid-paratyphoid vaccine and although considerable discomfort was experienced by the patients during the febrile attacks, there seemed to be no dangerous results and the course of the chorea was shorter than that treated by other methods. The changes in the chemical constituents of the blood caused by typhoid vaccine therapy included a diminution of the carbon dioxide content, a lowering of the chloride and phosphorus levels and a slight increase in the calcium content. It was the conclusion of the authors that the administration of typhoid-paratyphoid vaccine was a safer method and the treatment was easier to carry out than nirvanol. The results were better with the typhoid material than with nirvanol, since with the former therapy the subsequent recurrences of chorea were fewer and there were fewer unfavorable sequelæ.

**DELINQUENCY, JUVENILE.**—A survey of the incidence of predelinquent or problem children in the public schools of 10 cities was made by H. D. Williams (J. Juvenile Research 17 163 (July) 1933). Among 55,995 such children, 24 per cent had characteristics which might lead to delinquency. The size of the city seemed to have very little influence on the incidence rate, but some schools had 10 to 12 per cent of predelinquents and other schools none. The most common age was 10 to 15 years, the largest number occurring at 13 years, and much more frequently in boys (80 per cent) than in girls (20 per cent). The behavior problems occurred in children of all ranges of intelligence, from the feebleminded to those of superior mentality, the greatest number in those with intelligence quotients between 80 and 90. Some of the characteristics of the group were social maladjustment in 97 per cent, academic maladjustment in 83 per cent, defective home conditions in 77 per cent, irregular school attendance in 61 per cent, and physical abnormalities in 46 per cent. The boys were resistant to authority, were guilty of misconduct in school and annoyed other children, while

the girls seemed to suffer from inferiority feelings and were more often over-developed physically than were the boys of the group.

The types of juvenile crimes and certain *predisposing factors* were reviewed by M. G. Caldwell (*Ibid.* 17:179 (July) 1933) in a group of 341 juvenile delinquents observed over a 10-year period. Stealing was the most common offense, occurring in 42 per cent. of the group; sex offenses, which were most frequently committed by the girls occurred in 28 per cent.; misbehavior at home was the complaint in 9 per cent. The majority of the group were males (62 per cent.) and the modal age was 15 years. The great majority of delinquents, 80 per cent., were born of native parents and an additional 14 per cent. were born in this country of parents who were foreign born. Habitation seemed to have some influence on the incidence of delinquency, since 90 per cent. of the group came from urban centers and 9 per cent. from rural communities while the general population distribution is 60 per cent. urban and 40 per cent. rural. There was no significant preponderance of any religious belief among these boys and girls and, contrary to certain other statistical reports, only a relatively small percentage (29 per cent.) came from broken homes and in these homes there were 1 to 4 other children in most instances. Only 5 per cent. of the group were found to be mentally defective and previous court records existed in only 2 per cent. The author concluded that the average delinquent was a first offender, was native born, was normally intelligent, and came from normal homes of average size families living in cities. Many such children were thought to have been sent to special institutions and industrial schools before complete investigation had been made and before sufficient trial had been given the offender.

In the search for *causes* of juvenile delinquency, observations of *nutrition* of such patients were made by M. Molitch and A. K. Eccles (*J. Nerv. and Ment. Dis.* 78:123 (Aug.) 1933). The width of the iliac crests was measured and an index of skeletal development obtained by dividing this reading by the patient's height (both readings in centimeters). In addition, *mental tests* and a *behavior score* was obtained in each instance. Of the group of 554 delinquent boys studied, 27.4 per cent. were normal in mentality, 47.5 per cent. were slightly inferior, and 25.1 per cent. were definitely subnormal. The nutrition and development ranged from 25 per cent. below normal to 33 per cent. above normal and no relationship could be established between intelligence levels, behavior and nutrition. The undernourished group, however, were slightly less well equipped mentally and not so well adjusted socially.

In a special group of juvenile delinquents consisting of 100 boys who had been convicted of stealing automobiles, L. S. Selling (*J. Juvenile Research* 17:153 (July) 1933) believed that environment was the chief *etiologic factor*. Of this group, 81 per cent. were residents of the city, usually of the more congested districts, 30 had come from broken homes, 41 had fathers who were not working, 22 had had difficulties with their mothers, stepmothers or other members of the family, 62 had been truant from school. Factors which did not seem to be significant in this group were those of intelligence and race or nationality. The median intelligence quotient was 90, while that of a group of other juvenile delinquents was only 83. A frequent explanation given by the young auto thieves

was the desire for "riding around" and very few had any thought of selling the car. Emotional instability was not found to be a significant factor in this group of boys but the psychopathology was one of degree rather than quality and the result primarily of certain environmental conditions.

The type of cases observed by the staff of the clinic attached to the Children's Court in New York, are discussed by Helen Montague (Arch. Neurol. and Psychiat. 32:440 (Aug) 1934). According to their findings, the chief problems presented are emotional instabilities, arising from conduct disorders *following epidemic encephalitis or brain trauma, glandular disorders, physical defects* which cause the child to be ridiculed, *maladjustment in school, rivalry between siblings* in the home, *unwise and brutal punishment* by parents and the effects of *slum neighborhoods*. A type of problem that stands out clearly is that of the manual-minded boy who is a misfit both at home and at school. He compensates by acts of delinquency on account of his feelings of inferiority and becomes involved in gang-life, often with vicious adults. The schools are at fault in so far as they do not supply sufficient trade classes for these manually-minded boys and girls. Organized recreation is also lacking for these underprivileged children. More and more recreational clubs should seek out areas in the city in which delinquency is prevalent and break up gang-life by providing play activities of exciting and adventurous kinds. Definitely psychotic and feebleminded persons, particularly those with tendencies toward delinquency, are now segregated in proper institutions, but persons with abnormal personality defects who are known to develop criminal careers should also be segregated in a special type of institution for an indeterminate period for the same reason as are the feebleminded and the psychotic individuals. In the Children's Court, children of this type, for lack of proper placements, are sent to correctional institutions, with no beneficial results, later appearing in the prison groups.

The *physical defects* of a group of 282 juvenile delinquents were compared by A. Christie (*Ibid* 18:13 (Jan) 1934) with those of the same number of normal boys of a junior high school. Only 3.2 per cent of the delinquent group were free from physical defects, while 21 per cent of the normal group were physically sound. Poor oral hygiene, dental caries and defective tonsils occurred in much greater frequency in the delinquent boys than in the others. Defective vision was found in 28 per cent of the delinquent group and in 19 per cent of the high school group. In 6 of the delinquent patients, some organic lesion of the central nervous system was discovered. The frequency of skin diseases and certain other conditions in the group of delinquent boys was considered to be related primarily to their hygienic and economic environment. It was concluded that no one or group of physical handicaps could be assigned as a cause or a constant attendant of juvenile delinquency.

The *physical ability, intelligence, school achievement, and emotional stability* attitudes of 150 problem boys were compared with normal standards by H. K. Moore (*Ibid* 18:79 (Apr) 1934). Physical defects were not found to be more common among the problem children than among normal ones, but the average athletic ability for the former group did not reach the normal average. Mechanical aptitude and mental ages of the problem boys were generally found to be below

normal levels. The problem boys were less stable emotionally than the average boy and many of these psychoneurotic complaints seemed to be due to maladjustments or unfavorable conditions in the family life.

*Intelligence tests* of 3584 juvenile delinquents 9 to 16 years of age were compared with those of normal persons by K. H. Rogers and O. L. Austin (*Ibid.* 18:103 (Apr.) 1934). The mean I. Q. of the delinquent group was 82.24, which was below that of an average population of that age. There was some degree of selection of this group of delinquents, since the more intelligent children and those of families of high economic levels frequently escaped detention by the Juvenile Court. Retesting some of the same delinquent children during a period of 1 to 5 years, the authors found that the intelligence quotients were relatively the same or had a tendency to decline.

In the experience of C. C. Kirk and A. T. Hopwood (Ohio State M. J. 30:367 (June) 1934) only 11.2 per cent. of a group of 4586 mentally defective patients had shown any delinquent or criminal tendencies. As a measure of feeble-mindedness, the Binet-Simon tests were employed, and individuals with intelligence quotients of less than 75 were considered to be mentally retarded. Among a group of 514 defective delinquents, about 46 per cent had parents who were mentally retarded, 16 per cent. had histories of cerebral injury or disease at birth or in the early years of life, and 4 per cent. had had a history of convulsions. Tuberculosis, alcoholism and syphilis of the parents of these patients did not occur in significantly high percentages. In regard to social factors which may have contributed to delinquency, it was found that 25 per cent of the group were foreign born or were of the first generation of immigrants; 70 per cent. had come from cities of 25,000 or more; and 30 per cent had lost one or both parents from death, divorce or desertion.

Delinquent tendencies usually began at the ages of 10 to 14 years. Among boys petty larceny was the most common crime and among girls sex offenses were most frequent.

Emotional and character defects were common among this group of boys and indifference to any disciplinary measures was frequently observed. About 50 per cent of the group had certain psychopathic characteristics of moodiness, irritability, stubbornness and lack of attention. The desire to run away was manifested by 64 per cent of the 249 boys. Many of the patients who had been discharged from the institution had not been successful in their adjustment with society. Of a group of 72 males who were followed later in life, 55 per cent had persisted in their delinquent tendencies. It was the authors' opinion that special occupational and academic training should be given the juvenile delinquent in institutions from which running away would be very difficult. A parole system would then supervise the boy after discharge and if he repeated his antisocial acts and seemed incorrigible, permanent institutionalization should be required.

In his search for *characteristic mental attitudes* of a group of 825 young men who had committed minor offenses, A. Myerson (*Am J Psychiat* 13:501 (Nov.) 1933) concluded that the majority of such persons were extroverts who rarely examined their own actions. Most of the group were above the feeble-minded level of intelligence, but were lacking in curiosity in regard to human



motives or scientific principles. Interest in reading matter, music, art, government and politics was found to be very superficial. They rarely were skilled laborers and had but little desire to work steadily at one occupation to improve their skill. They had little desire to save for the future or to create a permanent home. In regard to sexual life, they rarely assumed the social responsibilities of providing for the family, nor were they, as a rule, members of organizations, churches or parties. Their emotions were shallow and reactions such as anger, joy and sorrow were usually very mild and short in duration. The author was inclined to believe that some of these shortcomings of this group of delinquents were due to defects of the germ plasm and possibly others were the result of unfortunate environment and training.

*Sex delinquency among girls* frequently seems to be the result of unsatisfactory home conditions. Such girls are usually placed either in institutions or in foster homes and the comparative merits of these two types of treatment of 96 patients were discussed recently by M. B. Barker and M. E. Rappaport (*Ment Hyg* 18:218 (Apr.) 1934). Community care in foster homes or wage homes was given 46 of this group and 50 others were recommended to institutions. Girls in the former group were somewhat younger, more intelligent and had less aggressive sex experience than those committed to institutions. The 46 girls who were returned to the community were observed over a period of 22 months. Of these, 29 were considered to have made good adjustments, 8 made fair adjustments, and 9 poor ones. Of these 9 poor adjustments, 5 seemed to be due to continued excessive sex interest, 2 to interference from the patients' families, 1 to a combination of these factors and 1 to a deeper-rooted mental difficulty. It was impossible to make comparative studies among those who were institutionalized, but there were 5 of this latter group for whom institutionalization was recommended but instead they were placed back into the community on probation. Three of these made good, 1 was definitely feebleminded, and the fifth had to be committed to an institution later. From these results, the authors concluded that community placement of sex delinquent girls could be recommended highly if sufficient and sympathetic supervision was available.

Alarmed by the increasing incidence of juvenile crime and the failure of finding any solution for its *prevention*, L. V. Briggs (*New England J. Med* 210:955 (May 3) 1934) sought for certain predisposing factors which might lead to such behavior. Many juvenile delinquents seemed to be seeking thrills only and learned the antisocial methods of gratifying this desire from street companions, popular literature, newspapers, radios, moving pictures and even the court rooms. Methods of prevention of juvenile crime, therefore, should include more rigorous censorship of the public news and picture organizations, careful observation of minor antisocial conduct in schools and especially the supervision of the adolescent boy or girl who leaves school to find work, so that a suitable environment may be established at once.

A critical survey of the *effectiveness of the present day methods of treatment* of the juvenile delinquent may be found in the first volume of the report of the Harvard Law School Crime Survey, written by S. Glueck and E. T. Glueck and reviewed briefly by R. C. Cabot (*Survey* 70:38 (Feb.) 1934). The book, which

is entitled "*One Thousand Juvenile Delinquents*," deals with subsequent histories of 923 of a group of 1000 who had appeared in a Juvenile Court during the years 1917 to 1922. Of this group, 88.2 per cent. had been arrested on an average of 3.6 times each, during the succeeding 5 years. In searching for causes of the delinquency and for factors which influenced the prognosis, the authors found that 13 per cent. of the group were feebleminded, 46 per cent. were dull, and only 41 per cent. were normal. A great majority of the group (95 per cent.) had been misbehaving at home or school before they committed crimes which brought them to the Juvenile Court. Delinquency was continued somewhat less frequently among boys who (1) had good parental discipline at home, (2) no history of previous misconduct, (3) no retardation of grade at school, and (4) began their delinquent conduct later in life. The failure of "cure" of any greater percentage of this delinquent group offered a challenge to the present organization of juvenile courts, parole systems and reform schools.

**DIABETES IN CHILDREN.\*—Treatment.—Diet.**—Judging from the reports on the treatment of juvenile diabetes, the use of what might be called normal or average diets is becoming more universal. The experience seems to be entirely satisfactory. Not only do the reports indicate that the children are kept more nearly in glycemic equilibrium and go into coma less frequently, but that they grow and develop, and in general lead more useful and happy lives. It seems a mistake to speak of high carbohydrate and low fat diets, but rather, if a comparison be made with the treatment of the past decade, of higher carbohydrate and lower fat diets. In placing too much emphasis upon the carbohydrate and fat, the protein may be neglected.

Thus, H. Medovy (Canad. M. A. J. 29:605 (Dec.) 1933), who reports excellent progress of 10 diabetic children on higher carbohydrate and lower fat feeding in contrast to his previous experience with the high fat diets, prescribed ample protein for his younger children while for one of the older ones he gave only 50 grams of protein to a 78-pound, 14-year-old child. This, at best, seems to be a minimal amount.

Similar criticism might also be applied to Bessau's method of feeding (carbohydrate, protein, and fat in similar proportions to those of human milk; protein approximately 8 per cent.) which is recommended by M. Weichsel (Jahrb. f. Kinderh. 141:25, 1933). E. Downie (M. J. Australia 2:367 (Sept. 16) 1933) recommends 2 to 3 grams of protein per kilogram of body weight, which would seem to afford a greater margin of safety.

**Ultraviolet Therapy**—The effect of ultraviolet therapy on the glucose tolerance, insulin requirements, growth and general health of diabetic children has been studied by N. Morris and D. C. Suttie (Brit. M. J. 1:614 (Apr. 7) 1934). Ten diabetic children between the ages of 7½ and 14½ years received exposures to ultraviolet light for a period of 1 year, and their progress, based on the above factors, was compared with 4 diabetic children who did not receive light therapy. No significant difference could be noted in the improvement in the two groups.

\* See also Section on METABOLISM

*Surgery.*—G de Takáts and G K. Fenn (Ann Int Med. 7:422 (Oct.) 1933) report the results of a **bilateral splanchnic nerve section** on an 18-year-old diabetic girl. The aim was stabilization and increase of sugar tolerance. There was an immediate drop to one-half of her pre-operative dose of insulin. This the authors attributed to an increase of insulin sensitivity. The increased sugar tolerance had persisted up to the time of the writing of the report, mentioned below, 10 months after operation.

In a subsequent publication, these authors together with R. A. Trump (*Ibid.* 7:1201 (Apr.) 1934) presented their method for the selection of diabetic patients who might be benefited by **splanchnic nerve section**.

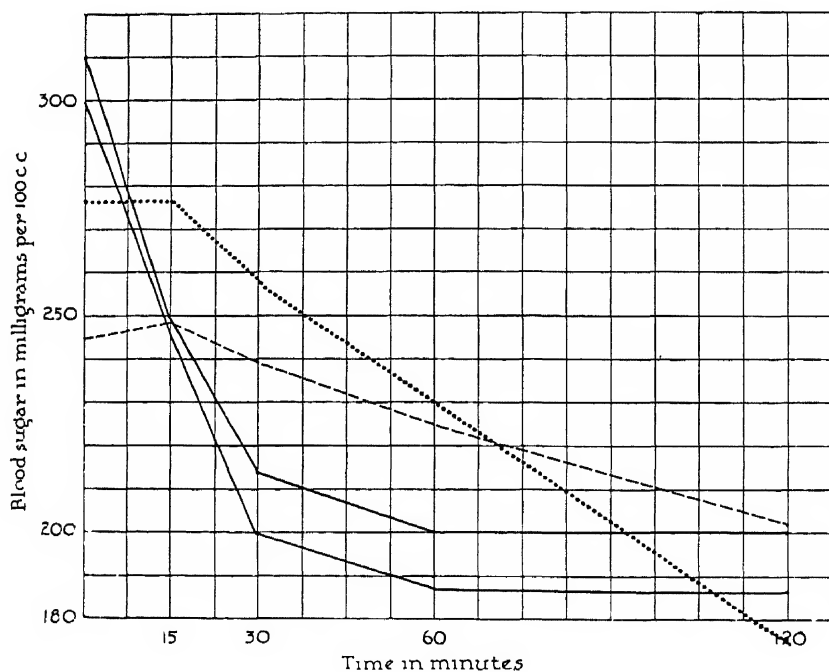


Chart I—Insulin sensitivity curves of Case 1 before and immediately after, and 12 months after bilateral splanchnic section. Interrupted line, before operation, straight lines, 1 and 2 months after operation, dotted line, 12 months after operation (Takats, Fenn and Trump Ann Int Med)

Children with the severe type of diabetes with unstable tolerance who have been diabetic for at least 2 years and adequately controlled for several months before the proposed operation and who have no x-ray or ophthalmoscopically detectable vascular damage could be considered as candidates for this operation, provided they were *insulin resistant* and showed a definite *inhibition of galactose hyperglycemia*, following the subcutaneous administration of ergot. The authors' reasoning is thus based upon the possibility of an extrapancreatic factor as a depressant of insulin activity in certain diabetics. This factor they believe may possibly be a sympathetico-adrenal one and may be measured, if present, by the sympathetic depressant effect of ergot upon galactose hyperglycemia.

Charts I and II show the insulin sensitivity curves and the effect of ergot upon the galactose hyperglycemia before and after splanchnic section.

The description of these two tests is as follows:

*Insulin Sensitivity Test.*—"A fasting blood sugar is determined from capillary blood by using the modified micromethod of Folin-Wu. Insulin is injected intravenously, using 0.01 unit of insulin per kilogram of body weight. Blood sugars are determined 15, 30, 60, 90, and 120 minutes after the injection. The patient is kept quiet during this time, preferably lying on a couch, in a room of even, non-extreme temperature. Excitement, fear or infection of any sort may vitiate the results. The diet should not be excessive in carbohydrate or fat."

*Ergotamine-Galactose Test.*—"A fasting blood sugar is determined by the modified micromethod of Folin-Wu and the individual is given 0.1 c.c. of gynergen (Sandoz) for every 10 kilograms of body weight subcutaneously. Fifteen minutes later, 40 grams of galactose (Pfanstiehl's pure d) is given by mouth in 250 c.c. of water, flavored with a little

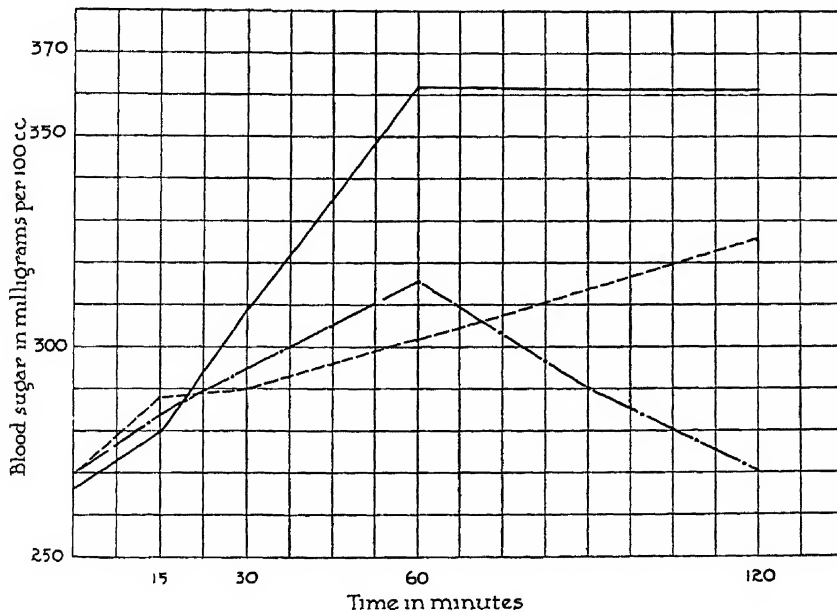


Chart II—Galactose hyperglycemia in Case 1, before and after splanchnic section. Straight line, galactose hyperglycemia without ergot, interrupted line, galactose hyperglycemia with ergot, both before operation, line and dot, galactose hyperglycemia without ergot after operation (Takats, Fenn and Trump. *Ann Int Med.*)

lemon juice. Blood sugars are taken at 15, 30, 60, 90, and 120 minutes after the ingestion of the galactose.

"A second dose of the gynergen is given 1 hour after the first dose. Prior to this test, a few days before, a galactose tolerance curve is determined with the same technic, but without the ergot."

*Clinical Investigation*—Interesting studies on the effects of various salts on carbohydrate metabolism and blood-pressure in diabetic children are being carried on by W. H. Thompson and I. McQuarrie (*Proc Soc Exper. Biol and Med* 31:907 (May) 1934). A constant diet and insulin dosage was given to a 15-year-old diabetic boy. The NaCl intake was varied and the urinary excretion of glucose and the blood-pressure were recorded during the period of study. A high NaCl intake was accompanied by an elevation of arterial blood-pressure from an average of 110/80 to 175/115 and the urinary excretion of glucose fell from a central level of between 60 and 70 Gm. to between 10 and 20 Gm. daily under the same conditions. When the NaCl intake was reduced to the control value of about 4 Gm. daily, the glucose excretion rose to its original

level and the blood-pressure fell to a normal value. Identical changes were produced in the same patient 4 times within a period of 3 months. No ketosis occurred. Similarly, the effects of sodium bicarbonate, sodium citrate and KCl were studied. The two other sodium salts had similar though less marked effects than the NaCl. The potassium salt had an opposite action in the one case in which it was given at the rate of 5 Gm. every 6 hours.

W. Sick and M. Weichsel (Monatschr. f. Kinderh. 58:383, 1933) have attempted to produce an acetonuria by means of insulin injections in controlled diabetic and in nondiabetic children. Thus, 15 units of insulin were given to nondiabetic children on adequate diets and on starvation diets respectively. No ketosis occurred in either instance. Likewise, no ketosis was produced in controlled diabetic children when their insulin dose was doubled and the diet maintained unchanged or when the child was starved for 5 hours and the insulin dose continued unchanged. They take this to be evidence that acetonuria is an indication of glycemie imbalance and that it does not result from an overdose of insulin.

**DIARRHEAL DISEASES IN CHILDREN.**—*Etiology.*—Bacteriologic studies by M. L. Cooper, H. M. Keller and B. Johnson (Am. J. Dis. Child 47:388 (Feb.) 1934 and 47:596 (Mar.) 1934) in infants with acute gastroenteritis have demonstrated that the *streptococcus* must be given greater consideration as a cause of this disease. In a series of 46 infants with acute diarrheal disease, the authors isolated a green-producing streptococcus from the stools of 65 per cent. There was an upper respiratory infection in 74 per cent. of the entire group and 65 per cent. of these had the same streptococcus in their intestinal tracts. Necropsy studies were made in 5 instances and this green-producing streptococcus was isolated from the small intestine of each. It is of interest that all of the infants who were infected only with this streptococcus had an average or below average white blood count.

Animal experiments were carried out and intestinal lesions were produced in rabbits and monkeys by intravenous injections of this organism. The same streptococcus was, in turn, isolated from the infected animals and other animals were similarly affected by it. A similar streptococcus isolated from the throat of one of the patients with an acute upper respiratory infection produced the same intestinal lesions in injected animals. It was possible to protect the experimental animals with specific immune serum.

The chief characteristic of this streptococcus is its formation of unusually small colonies. The production of a green color on media is secondary in importance. Furthermore, the morphology of the microorganism does not seem to differentiate it from other streptococci. For this reason the authors suggest that the term "*streptococcus micro-apoikia*" (small colony) be employed to distinguish this group of streptococci, and that suitable terms be added to connote their peculiar pathogenic properties. For example, this strain would be designated as "*streptococcus micro-apoikia enteritidis*."

Serum from goats immunized against this particular strain of streptococcus (unpublished data; personal communication) has been used with favorable

results in a few infants with acute enteritis. The injection was followed by a prompt fall in the temperature to normal and a subsidence of symptoms with rapid convalescence

**Intracellular Loss of Fluids and Electrolytes.**—One of the essential steps in the treatment of severe gastroenteritis is the correction of dehydration. The extent of the dehydration is generally considered to be determined by the quantity of interstitial fluid lost as the result of vomiting and diarrhea. A. M. Butler, C. F. McKhann and J. L. Gamble (*J. Pediat.* 3:84 (July) 1933) have shown that there is, in addition, marked loss of water and electrolytes from the tissue cells themselves. Since the electrolytic content of the intracellular fluid is quite different from that of the extracellular fluid (a much higher concentration of potassium and phosphate in the intracellular fluid in contrast to the higher concentration of sodium and chloride in the extracellular), the needs of replacement are different. The loss of interstitial fluid is combated by the administration of **physiologic salt solution** or perhaps better by **Hartmann's solution** "which copies in detail the composition of interstitial fluid." The authors suggest that some of the failures in treatment may be due to the inability to replace in sufficient quantities the loss of the intracellular materials, potassium and phosphate. Since repair solutions must be placed in the vascular or in the interstitial compartment, the solutions cannot contain with safety such of the intracellular materials as potassium and phosphate at concentrations higher than their existing small values in extracellular fluids. It is to be hoped that investigation in this direction will be continued and that means of treatment for this phase of the dehydration of diarrheal disease may result.

**Treatment.**—*Administration of Fluids; Acid-base Balance*—The treatment of the more severe diarrheas of infancy, as carried out in the St. Louis Children's Hospital, is summarized by W. M. Marriott, A. F. Hartmann and M. J. E. Senn (*J. Pediat.* 3:181 (July) 1933) as follows:

1 **Total restriction of food** for 12 to 48 hours or more, depending upon whether or not diarrhea tends to continue in spite of food restriction

Small amounts of acidified and buffered water are offered in order to keep the stomach and intestines sufficiently acid to prevent the growth of intestinal organisms. This solution is prepared as follows:

R	<i>Lactic acid, U. S. P.</i>	. . . . .	℥ss (15 c c).
	<i>Sodium hydroxide, 10 per cent</i>	. . . . .	f5v (20 c c).
	<i>Water to</i>	. . . . .	f℥iiss (100 c c)

Before use, the solution is diluted 1 part to 10 with water. The mixture may be sweetened with saccharine.

2 **Administration of an isotonic solution of sodium *r*-lactate** to relieve the acidosis and at least partially relieve the dehydration. If the acidosis is severe, the usual dose of sodium lactate is 10 c c ( $2\frac{1}{2}$  drams) of a molar solution per kilogram of body weight, diluted with 5 volumes of sterile distilled water. One-third to one-half is injected intravenously, in order to restore as quickly as possible diminished blood volume. The remainder is given subcutaneously or intraperitoneally.

3 Administration of physiological buffer salts solution (**Hartmann's solution**) parenterally.

4 Administration of **dextrose solution** to furnish fuel, to relieve ketosis, and to aid in reestablishing the glycogen reserves of the body. The dextrose solution may be given subcutaneously in 6 per cent. solution or by continuous intravenous drip in 10 per cent solution. In either instance, the dextrose solution may be diluted with an equal volume of physiological buffer salts solution. The rate of intravenous injection should not exceed 3 c c per kg of body weight per hour.

5 Administration of **citrated whole blood**. Blood transfusions should not be given until after the fluid balance has been restored.

6. After the preliminary starvation period feedings are resumed by offering small amounts of **Dryco** or **dried protein milk**, diluted 1 to 10 with the buffer mixture described under "1. Total restriction of food . . . ." As the patient improves and the diarrhea becomes less, the dried milk dilution may be increased (1 to 8), carbohydrates being gradually added in the form of **Karo syrup**. After approximately 6 per cent carbohydrate has been added to this formula and the patient is taking a reasonable amount for his age, **evaporated milk** diluted with an equal volume of buffered solution or 1 per cent **lactic acid**, and with the addition of 5 to 7 per cent of **carbohydrate** may be substituted for the dried milk formula.

A somewhat simpler treatment is followed in the Jewish Hospital of Brooklyn by H. Cohen, P. R. Miller and B. Kramer (*Ibid* 3 299 (Aug.) 1933). In a small group of infants who were exceptionally well studied from a chemical standpoint, they had a comparatively low mortality (2 of 9 infants) on the following regime:

1 **Complete starvation**, for from 12 to 24 hours, depending upon the amount of vomiting and diarrhea.

2 Administration of 600 to 1200 c c of 5 per cent **glucose in normal salt solution** per day by continuous intravenous drip.

The intravenous flow was maintained until diuresis was well established, dehydration corrected, and until toxicity had disappeared.

3 Following the starvation period, small amounts of 5 per cent **glucose** were given **by mouth**.

4 A formula of **reinforced protein milk** was started after about 24 hours, if there was definite diminution of toxicity and improvement in the diarrhea.

Acidosis, when present, was controlled both clinically and chemically without the use of sodium bicarbonate injections. Blood transfusions were not given routinely, but only for special indications. Because of the small number of cases treated in this manner, the authors are not willing to draw definite conclusions regarding its efficacy.

The **continuous intravenous administration of fluids** has been found by R. A. Lyon, J. G. van Dermark and A. Graeme Mitchell (*Ohio State Med. J.* 30:227 (Apr.) 1934) to be an efficient method to combat the dehydration and toxicity of severe diarrhea and marked improvement was generally noted after

500 to 1000 c.c. of fluid had been given. The disappearance of dehydration and the increased tolerance for liquids by mouth were the two most striking clinical observations. The treatment was less effective in infants with severe respiratory infections, especially pneumonia. The chief dangers of this method are (1) too rapid or irregular flow of the solution, (2) the development of phlebitis, (3) dilution of the blood proteins with resultant edema, (4) circulatory failure. Careful observation and immediate adjustment or removal of the apparatus, when such symptoms occur, will prevent serious complications.

*Restoration of Kidney Function.*—It has been shown that one of the important causes of acidosis accompanying the acute stage of gastroenteritis is decreased kidney excretion, since it is responsible for retention of acid ions in the body. For this reason E. Marples, H. Cohen and H. Talamo (Am. J. Dis Child. 47:331 (Feb.) 1934) believe that the primary aim of the initial treatment should be the restoration of an adequate flow of urine. They have injected **hypertonic solutions of dextrose** (usually 10 per cent) intravenously in order to accomplish this purpose. If, in addition, **saline solution** is administered **subcutaneously** the three requirements of immediate treatment, the furnishing of fluids and electrolytes, and the stimulation of renal function, are met. They report improvement in clinical condition and in the acid-base status of the blood following the use of this method of treatment.

*Diet*—A comparison of treatment of diarrhea in children with **citric acid milk**, with **lactic acid milk** and with the **Moro apple diet** has been made by L. Lennhoff (Monatschr. f. Kinderh. 58:130 (June 14) 1933). He could detect no essential differences in the effects of the two acid milks. Children treated with the apple diet were given apples exclusively for 48 hours after a preliminary starvation period of 12 to 24 hours during which only tea was given. The apple diet was followed by the administration of lactic acid milk. No differences in the improvement of the general condition, the reduction of fever, the disappearance of the vomiting or of the tenesmus could be noted in children treated in this way. However, blood and mucus disappeared from the stools more quickly and they regained their normal consistency more rapidly. The author states that the apple diet is not suitable for nurslings of less than 8 months of age.

E. Urbanitzky (Munchen med Wchnschr 80:1219 (Aug. 4) 1933) has used the **apple diet** in small infants with diarrhea as well as in older infants and children. Ten infants less than 6 months of age, 12 between 6 months and a year, and 25 less than 2 years of age who were suffering from various types of acute and subacute intestinal disorders responded well to the use of an apple preparation. A pure apple powder was used instead of the fresh ripe fruit. The youngest infants were first given tea with 4 per cent apple powder added. This was followed with a milk mixture to which was added 5 to 6 per cent of the apple powder.

In addition to the use of **raw ripe apples** (Heisler-Moro) and **bananas** (Fanconi) for the treatment of acute diarrheal disturbances in children, M. Schacter (Arch. de méd d enf. 37:139 (Mar.) 1934) reports similar good results with **raw pears** and **apricots**. They should be thoroughly ripe and are



prepared in the same manner as apples (peeled, cored and pulped) He believes that the mechanism of action of all these fruits is the same and that the organic acids seem to be responsible for the good results

**DIPHTHERIA.—Mortality.**—In the annual report of diphtheria mortality the rate in 1933 in large cities of the United States (J A M A 102:1758 (May 26) 1934) was 2.32 per 100,000 population which was the lowest figure for the last 10 years. An unusually large number of cities, 11 in all, had no diphtheria deaths during the year 1933. The cities in the New England States continued to have a declining rate and the cities of the Middle Atlantic States had a marked diminution of deaths from diphtheria. The cities of the North Central States had lower rates generally and especially noteworthy reductions occurred in Chicago and Detroit. The Mountain and Pacific cities which led the country with lowest death rates from diphtheria until 2 years ago, continued to make a fine showing. Certain cities of the Southern States had higher rates than cities of the North and very little reduction of mortality has occurred there in the last few years.

In comparing the mortality rates of scarlet fever and diphtheria during the last 75 years in England and Wales, L. Cobbett (Brit M J 2:139 (July 22) 1933) noted that that of scarlet fever had diminished to almost zero, while that of diphtheria had diminished more gradually and was still quite high. The author believed that the early administration of antitoxin was still the most important factor in the reduction of the death rate of this disease.

**Race Incidence.**—Variations of incidence of diphtheria due to racial differences has been a subject of numerous investigations. Recently, J. D. Black (Am J Hyg 19:734 (May) 1934) made a statistical survey of the susceptibility of the negro and white races. In the summary of his investigation he stated that the mortality rates were lower for negroes than for white people during the years 1915 to 1924 except in certain large cities, but for children under one year of age and for adults, the mortality rates were greater in the negro race. Morbidity statistics indicated the same age distribution of the disease. Carriers of diphtheria bacilli have been found in equal numbers in both races. Some of the data previously reported on the incidence of negative Schick reactions have demonstrated an equal distribution between the races, while other figures have indicated that there are smaller percentages of immune negroes than whites. E. Grasset and A. Perret-Gentil (Compt rend Soc de biol 113:1457 (July 22) 1933) performed Schick tests on negroes in South Africa and found positive reactions in various age groups in the same relative numbers as in European groups. The greatest percentage of positive reactions were found in children 3 months to 3 years of age (47.05 per cent.). At the age of 6 years the percentage of positive reactions had dropped to 9.09 and ranged between 3 and 6 per cent. in the older age groups. Among the 276 natives not in contact with white civilization, 6.16 per cent. had positive reactions and of 287 living in Johannesburg, 10.45 per cent. were positive. The authors concluded that the diphtheria immunity of the native African in that locality was acquired and not inherent.

In a subsequent investigation (*Ibid.*, p. 1460) the antitoxin content of the blood of 172 of the same group of individuals was found to be more than  $\frac{1}{5}$  unit in all but 7.56 per cent. Clinical diphtheria of the natives was observed most frequently in children 1 to 5 years of age, and the authors believed that the conditions and methods of acquiring immunity in the natives were very similar to that of persons living in congested areas of Europe.

**Bacteriology.**—During the last few years, certain English bacteriologists have been able to classify strains of diphtheria bacilli into 3 general groups, according to their morphologic and cultural characteristics. The *gravis* strain was found in cases of severe clinical diphtheria and the *mitis* strain in mild infections. The third was intermediate between the other two. Other workers in other localities have not been able to substantiate these findings. Recently, however, D. T. Robinson and F. N. Marshall (*J. Path. and Bact.* 38:73 (Jan.) 1934) have been able to classify practically all strains which they have isolated from patients in the area of Manchester, England. The *gravis* strains were most frequently obtained from severe and fatal diphtheritic infections. They seemed to have produced clinical diphtheria in Schick negative persons and to have invaded tissue more readily than the *mitis* strains. Clinically, however, there was nothing in the appearance of a diphtheritic membrane that would have indicated which type of bacillus was the etiologic agent.

In a report made by H. M. Leete, J. W. McLeod and A. C. Morrison (*Lancet* 2:1141 (Nov. 18) 1935), the incidence of diphtheria in Hull, England, in 1932, was more than 4 times greater and the mortality almost 6 times greater than in 1923. Since the toxemia and severity of the disease often seemed out of proportion to the clinical signs of infection in the nasopharynx, cultures of the bacillus were made in order to determine differences in virulence among the microorganisms. In 310 patients with diphtheria of varying severity, 59 per cent had *gravis* strains of the bacillus and of a group of 40 fatal cases, 35 had this type of infection. Intermediate strains of the bacillus were isolated from patients with moderately severe diphtheria and *mitis* types occurred generally in the mild cases. Since the *gravis* strains of the bacillus seemed to produce toxin so rapidly in nonimmune subjects, active immunization was recommended as the most effective method of combating the epidemic.

In the investigation of 510 strains of diphtheria bacilli, H. S. Carter (*J. Hyg.* 33:542 (Nov.) 1933) found that they usually fell into 3 general classes, according to the appearance of the colonies and the ability to ferment starch solutions. These strains were stable and had definite characteristics. The 2 milder types were much more frequent in patients with the mild clinical forms of the disease and such patients yielded to antitoxin treatment much more readily than patients infected with the most virulent type.

A method for *rapid culture of diphtheria bacilli* was devised by A. Solé (*Wien klin. Wchnschr.* 47:713 (June 8) 1934). He employed a modification of a method reported by Folger many years ago.

A sterile swab was dipped in sterile horse serum until the cotton was saturated and then it was pressed against the side of a bottle and heated over a flame until vapors came off and the serum was slightly coagulated. This swab had to be used at once to obtain the culture.

from the nasal and pharyngeal secretions of the patient. It was then placed in a sterile tube and incubated at 37° C. After 2 hours the microorganisms could be scraped from the swab on to a slide to be examined microscopically. In 80 per cent of trials this amount of incubation was sufficient to make a satisfactory reading and his results compared favorably with those obtained by the customary methods. It was thought to be advisable to continue the incubation in all cases in which the diagnosis was still doubtful at the end of the 2-hour interval.

**Clinical Aspects.**—A new and more *accurate classification* of various grades of clinical diphtheria infections was thought necessary by B. Schirwindt (Jahrb. f. Kinderh. 141:318 (Jan.) 1934), who has been dealing with diphtheria in the Soviet Union and especially in Moscow. In his opinion the toxic forms should be divided into the (1) *hypertoxic group*, with a very rapid and stormy course of severe toxemia and death occurring by the fourth day, (2) the *typical toxic group*, with edema of the neck, usually with kidney involvement and disturbances of the nervous and circulatory system. This group might be subdivided into hemorrhagic and gangrenous types (3) The *subtoxic group*, with less severe symptoms. No one symptom was characteristic of any of these groups but both the local and general symptoms were to be taken into consideration. Under observation were 205 patients of the toxic type of which 108 were 2 to 5 years of age and 83 were 5 to 10 years old. Three patients were classified as hypertoxic, 110 as typical toxic, and the remainder, 71, as subtoxic. Involvement of the nose usually occurred in the toxic group, and was present in 80 per cent of this series. Laryngeal infections were rather more rare but nephritis was common (82 per cent). Myocarditis, occurring late in the disease, usually after the third week, was less fatal than that developing earlier. Postdiphtheritic paralysis occurred in 24.4 per cent of this group of patients, usually at the end of the second week of the disease. Toxic symptoms sometimes appeared at the onset of the disease and occasionally on the second or third day. Of poor prognosis was the occurrence of hemorrhage at the site of the inoculation of serum. Death occurred in 21.6 per cent of this group, usually in the second week, but rarely after the third week. Only a few of the toxic patients had had any treatment before the third day of the illness and the importance of early treatment was emphasized.

The frequent occurrence of severe forms of diphtheria in central and eastern Europe led F. Bormann (Ergebn. d. inn. Med. u. Kinderh. 45:433, 1933) to employ the term *invasive diphtheria*. He believed these types to be *mixed infections*. Streptococci could be isolated from the blood of 31.2 per cent of his patients with these severe diphtheritic infections and in only 7.5 per cent of patients with milder and pure diphtheritic infections. In the throats of such patients, staphylococci, Friedlander's bacilli and Vincent's organisms were found.

In search for an explanation of the malignant types of diphtheria, A. Stróé (Arch. f. Kinderh. 100:86 (Sept.) 1933) reviewed 17 cases of this type which he had observed. From a clinical standpoint, these patients had double infections with dirty gray membrane formation and underlying gangrenous, necrotic lesions. At the same time there was an epidemic of severe scarlet fever with gangrenous lesions in the throats and it was thought that there might be some

connection between the two types of infection. In the direct smears of the membranes of the diphtheria patients there were many microorganisms, but only the diphtheria bacillus and streptococcus or staphylococcus grew in aerobic cultures. In anaerobic cultures other bacilli were discovered and he concluded that the two former bacteria produced membranes in the throats, while the anaerobic bacilli simultaneously produced the gangrenous lesions. Treatment with large doses of **antidiphtheria** and "**antigangrene**" sera was thought to be responsible for the recovery of 16 of the above group of patients. One of the children who died of a heart complication had received no treatment until the sixth day of the disease.

*Diphtheritic nasal infections* were observed rather frequently in young infants in a children's home in Odessa by H. Stux and Z. Zirulnik (Acta. paediat. 15: 26 (Sept.) 1933). During a 5-year period 106 cases of diphtheria in infants under one year of age were observed, which represented 6.4 per cent. of the total number of diphtheria patients. Of the group, 89 had nasal infections and 16 skin infections. Only once did pharyngeal diphtheria occur in this age group. These infections occurred most frequently in the winter months, from November to February. Other infections, such as gripe and nasopharyngitis, seemed to predispose to the diphtheria invasion and in 11 instances smallpox vaccination immediately preceded the infection. Exudative skin lesions also played a causative rôle. The nasal and skin diphtheritic infections were usually mild, led to no latent complications, and tended to be subacute or chronic in their course. Middle ear infections followed nasal diphtheria in 5 patients and were severe, occasionally leading to mastoiditis or subperiosteal abscesses. Of 27 instances in which virulence tests were made, 25 gave positive results. The Schick reaction was found to be of little value in making the diagnosis, but serum therapy in average doses of 400 units was found to be effective in the treatment. In the majority of these nasal infections the bacilli were harbored for a long time. At the end of 2 months, 40 per cent. of the infants still retained the bacilli and after 3 months, 15 per cent. were still carriers. Active immunization of infants under 6 months of age was thought to be impossible, but treatment of the general nutrition and improvement of the resistance of the infants were emphasized. If necessary, passive immunization was given at that age and attempts to produce active protection were postponed until the age of 6 months had been attained.

**Unusual Clinical Forms of Diphtheria.**—*Primary diphtheria of the tracheobronchial tree* was observed in 2 young adults by N. Toomey (Radiology 21: 130 (Aug.) 1933). In the absence of membrane in the larynx, pharynx, or nose, early diagnosis was difficult. Signs of toxemia and obstruction of breathing suggested the diagnosis and the x-rays showed evidence of a membrane before positive cultures could be obtained from the expectorated material. One of the above patients died in spite of the administration of large doses of antidiphtheria serum.

Unusual sites of diphtheritic lesions were observed by P. Eivine and N. Schoenbaum (Arch. de méd. d. enf. 37: 337 (June) 1934). Among 91 patients, diphtheritic lesions of the *skin* were observed in 25 instances or 27.5 per cent. of the group. Occasionally, these skin manifestations did not assume typical

forms of diphtheria, but resembled intertrigo, impetigo, varicella, abscesses and various other lesions. Only where there was a break in the skin surface did diphtheria bacilli invade and then the infection was usually so atypical and localized that the danger of contagion seemed to be slight. Diphtheria of the *eyes* was usually found to be bilateral. Similar infections of the *ears* resembled the usual draining otitis media.

In regard to treatment of such diphtheritic lesions, the authors found that the injection of 8,000 to 10,000 units of **antitoxin** usually produced a cure except in the case of conjunctivitis in which case 80,000 to 100,000 units in divided doses seemed to be necessary.

*Vulvovaginal diphtheria*, secondary to tonsillar and pharyngeal diphtheria, was described by M. J. Wallfield and A. M. Litvak (J. Pediat. 5.756 (Nov.) 1933). A membrane extended over the labiæ and caused them to be adherent. Cultures obtained from this membrane and from the throat were positive for diphtheria bacilli. After intensive **antitoxin** therapy the lesions healed completely. Two instances of diphtheria of the vulva were also observed recently by K. Oxenius (Kinderarztl Praxis 5 251 (June) 1934).

*Urethritis* due to diphtheria is a very rare occurrence. Such an infection in a man 45 years of age was described by N. E. Berry (J. Urol 30 263 (Aug.) 1933). The lesion was membranous in type, involved the anterior portion of the urethra only, and apparently was cured by the administration of **antitoxin**. A year after the first infection, a second attack occurred and healed after local treatment and intramuscular doses of antitoxin. Although the microorganism was culturally and morphologically a typical diphtheria bacillus, it was not virulent and possibly belonged to a xerosis group.

An unusual distribution of diphtheritic lesions was observed recently by R. H. Cantrell (J. A. M. A 102:1295 (Apr 21) 1934). A woman, 28 years of age, developed first an ulceration of the *vulva* and *perineum*, and then excoriations under the *breasts* and lesions on the *tongue* and *tonsils*. Diphtheria bacilli were isolated from all of these areas. Large doses of diphtheria antitoxin were administered but the patient developed a pneumonia and died.

**Complications.**—The mechanism of the effect of diphtheria toxin on the *blood-pressure* has been investigated recently by P. Regniers and G. de Vleeschouwer (Compt rend. Soc de biol 114.1394, 1933). In their observations of 40 dogs injected with diphtheria toxin they noted a fall in the blood-pressure after a period of about 3 hours when 25 minimal lethal doses were injected, and a longer latent period when smaller doses were given. In these animals the vasoconstrictor action produced in the carotid sinus by occlusion of the common carotid was diminished and this condition occurred an hour or more before the general fall in arterial pressure was observed. At the same time and in later periods of severe intoxication, no diminution of the peripheral vasoconstrictor mechanism, as determined by excitation of the splanchnic nerves, was observed. Adrenalin given intravenously had little or no effect in raising the blood-pressure of the severely intoxicated animals. However, the injection of a 1 per cent solution of potassium chloride into the third ventricle of the brain, which is a procedure usually followed by considerable vasomotor response,

had little or no effect on this series of animals. The authors concluded that the peripheral vasomotor reflex mechanism was not primarily involved in diphtheria intoxication, but that the chief reaction consisted of a depression of the central vasomotor centers.

Effects of diphtheria intoxication on the *chemical constituents of the blood and internal organs* were investigated by H. Yannet and D. C. Darrow (J. Clin. Investigation 12:767 and 779 (Sept.) 1933). They observed the results of intravenous injections of diphtheria toxin in fasting rabbits and found that severe toxemias cause a *hypoglycemia* and an *increase of the amino-acids and nonprotein nitrogen* in the blood. In mild toxemias the blood sugar was increased in animals surviving 5 to 7 days and the amino-acid nitrogen was slightly increased. The nonprotein nitrogen greatly increased. It was thought that the azotemia was due to kidney damage, the amino-acid increase to hepatic damage, while the blood sugar depended on the relative amount of injury to the liver. *Lactic acid* determinations gave variable results, although there seemed to be less tendency for an increase of this acid in the blood during mild infections than in the severer ones.

The *liver glycogen* was found to be diminished in the severe toxemias of these animals, although that of other tissues, such as the heart and skeletal muscle, was unchanged. The injection of glucose was followed by a diminution of hepatic glycogenesis and this process was unaltered by insulin injections. The failure of carbohydrate metabolism in these animals was thought to be due, in part, to disturbed liver function.

In a study of 5 patients who died of diphtheria, D. Combiesco (Compt. rend Soc de biol. 115 670, 1934) found no gross lesions of the *pancreas*, but certain histologic changes. In 2 cases, there was evidence of small hemorrhagic areas in the interlobar spaces, in the acini of the glands and occasionally in the islands of Langerhans. There was frequently a dilatation of the arterioles of the organs and areas of necrosis about the capillaries. There was never any necrosis of the acini.

*Lesions of the facial nerve* due to diphtheritic infections were observed in 4 patients by H. Seckel (Deutsche med Wchnschr 59 1918 (Dec 29) 1933). In a much larger number of diphtheria patients (about 16 per cent of a group of 330), Chvostek's sign was positive and later became negative. In 3 patients with definite unilateral paresis of the facial nerve there seemed to be a stage of irritation and pain accompanied by a positive Chvostek sign on both sides, followed shortly by a decrease in intensity or disappearance of the sign on the side which was becoming paralyzed and no change or an increase in intensity of the sign on the opposite side. These two stages together lasted for 16 to 26 days and then the Chvostek sign was sometimes positive on the paralyzed side and tended to disappear on the opposite side. Later, as the facial nerve function returned to normal, the Chvostek sign disappeared from the affected side also.

**Treatment.**—The *dosage* of *antitoxin* determined from the observation of the results of serum therapy in a group of 198 patients with diphtheria of varying severity by Willemin-Clog and Muller (Bull Soc de Pédiat de Paris 32 99 (Feb) 1934) was 400 units per kilogram ( $2\frac{1}{5}$  lb) of body weight for mild

infections, 800 units per kilogram of body weight for moderately severe ones, and for severe cases 1200 to 1500 units per kilogram. Of this amount, 10 c.c. were given intravenously and the remainder in the muscles or subcutaneous tissues. If the patient did not show improvement within 24 hours, serum injections were repeated. In cases of suspected diphtheria, 400 units of antitoxin per kilogram of body weight were advised, and for croup 800 units per kilogram unless there was evidence of tracheobronchial involvement, which was treated as a very severe infection. In a comparison of two groups of patients, one group with the moderate or severe types of infection treated with large doses and the other group treated with moderate or small doses, complications were noted to have occurred more than twice as frequently among those receiving the latter amounts of antitoxin.

In malignant types of diphtheria, F. Barber (*Monatschr. f. Kinderh.* 60:224 (June) 1934) observed that large doses of diphtheria antitoxin seemed to have no effect on the disease. He reduced the amount and gave to 42 children with malignant diphtheria only 1500 to 10,000 units of antitoxin as an initial dose and followed this for the next 3 to 5 days with several doses a day of 5 to 10 c.c. of normal horse serum until the membrane and edema of the throat had begun to disappear. The mortality of 59.5 per cent was quite comparable to that obtained with large doses of 50,000 to 100,000 units or more of antitoxin. By neither method, however, were the results from treatment of malignant diphtheria entirely satisfactory.

The length of time which antitoxin remains in the blood of those who have been given the serum as treatment of the disease was determined by G. Ramon, R. Debré and J. Bernard (*Compt. rend. Soc. d. biol.* 114:1089, 1091, 1933) from the observations of 34 children who had diphtheria infections of varying severity. Antitoxin had been administered in doses of 12,000 to 180,000 units on the first to the fifth day of the disease. No evidence of appreciable amounts of antitoxin in the urine could be found. In the blood, the antitoxin remained for 20 to 80 days, but the amount varied from 5 to 32 units. No relationship between the antitoxin content of the blood and the severity of the infection or the quantity of antitoxin given could be discerned. The quantity of antitoxin in the blood rose, after the serum administration, within a variable length of time which was independent of the dosage or the weight of the patient. During the period of observation of 20 to 30 days, the serum did not fall below  $\frac{1}{10}$  unit of antitoxin per c.c. of blood, regardless of the number of injections or the dosage.

In certain instances, the patients who received the greatest amount of antitoxin had the least amount in the blood on subsequent examination. In general, there were 2 types of response to the antitoxin injection among a group of 18 patients studied. In one-half of the group, the antitoxin of the blood rose rapidly in 24 to 48 hours and descended rapidly either in a very short time or after 8 to 10 days. In the other group the antitoxin content rose slowly, to reach its maximum in 8 to 22 days and often remained high for several weeks before it slowly receded.

There was no explanation found for these differences in reaction but it was concluded that the antitoxin in the great majority of instances became sufficiently concentrated in the blood and within a sufficiently short length of time to neutralize all the toxin present, and that it remained there long enough to assure convalescence during the infection with the diphtheria bacillus.

Similar variations in the antitoxin content of the blood were observed in patients with serum sickness who excreted the toxin rapidly and in patients with high antitoxin titers who had received large doses of serum treatment, according to the report of P. Zoelch (*Ztschr. f. Kinderh.* 56: 358 (May) 1934). He believed that the development of antitoxin in a patient was influenced by the ability of the body to excrete antitoxin. The tissues as well as the blood probably influence the toxin antitoxin combination. Most of the treated diphtheria patients have higher titers of antitoxin in the blood during convalescence than the Behring threshold. The occurrence of paralysis in diphtheria was apparently entirely dependent upon the time of administration of the serum in relation to the onset of the illness, because the serum did not seem to pass into the central nervous system for at least several days. Serum given intraspinally apparently had no beneficial therapeutic effect. Human convalescent serum in the treatment of mild or moderate cases of diphtheria was thought to be beneficial chiefly because of the presence of small amounts of antitoxin, although the factor of the nonspecific value of the serum could not be ignored.

Blood antitoxin determinations were made by D. L. Klein, H. B. Cushing, A. Goldbloom and E. V. Murphy (*Canad. M. A. J.* 29: 593 (Dec.) 1933) in a group of 10 children who had had diphtheria 6 months to 4 years previously and had received antitoxin as part of the treatment. In 7 instances there was sufficient antitoxin in the blood to afford protection against another attack of the disease but 3 patients had amounts of blood antitoxin which are usually thought to be insufficient to give protection. The authors were inclined to believe that these patients had considerable tissue immunity and could develop antitoxin rapidly under certain stimuli. The children who had the most severe clinical diphtheritic infections seemed to possess the least antitoxin in the blood. The administration of antitoxin therapy during the illness had no apparent effect on the subsequent immunity developed by the patients.

**Blood transfusion** has been employed in the treatment of diphtheria with considerable success. H. Dimmel (*Med. Klin.* 29: 1578 (Nov.) 1933) gave transfusions to 16 children, 2 to 13 years of age, who had malignant diphtheria infections. Other treatment, such as **antitoxin**, was given as usual. The mortality rate in this small group was 35 per cent as compared with 66 per cent of a control group and the immediate effects of improvement of the general condition were noticeable. The beneficial results of the blood transfusion did not seem to depend entirely on the amount of antitoxin in the donor's blood, but on some other factors which were not determined. Although the number of children in this experiment was small, the author was convinced that the therapy was beneficial for patients with malignant diphtheria.

The value of blood transfusion of toxic diphtheria patients is due to some additional factor than its antitoxin content alone, in the opinion of H. Auffen-



berg (Kinderärztl Praxis 5.97 (Mar.) 1934). The beneficial effects were often slow in manifesting themselves but 2 of a group of 7 patients with malignant diphtheria were thought to have been saved by this treatment. Nine other patients with toxic diphtheria who were treated in this manner recovered and 6 others with severe diphtheria recovered with no serious complications, which were better results than those obtained in other groups not treated with transfusion.

**Blood transfusions** have also been used by H Baar and H Benedict (Acta paediat 16:433, 1933) in the treatment of patients with malignant diphtheria characterized by cervical gland enlargement and edema, by a stuporous toxic condition, and by some evidence of cardiac disease. Human blood was given in addition to the regular **antitoxin** therapy of 10,000 to 40,000 units to 43 such patients. Reactions consisted of chills in a few instances. The edema of the neck disappeared first and the membrane of the throat and the cervical adenopathy disappeared more slowly. It was difficult to evaluate the results because of the variation of individual patients and their infections. The number of patients was small, but a comparison with mortality rates of those treated with antitoxin alone showed that the number of deaths had been reduced. The authors felt justified in claiming that a 50 per cent reduction in the mortality rate of patients with malignant diphtheria might be expected from the treatment with human blood. It was their opinion that some other factor of body resistance and tissue affinity rather than the antitoxin content of a patient's blood alone was responsible for the invasion of severe diphtheria infections.

A warning against too liberal use of antitoxin and human blood in diphtheria patients with *cardiac complications* has been sounded by P Kiss (Arch f Kinderh 101 84 (Jan ) 1934). Many clinicians have advocated intravenous therapy in certain individuals with diphtheria in order to combat peripheral collapse of the vascular system and to restore the normal blood-pressure. In 2 children who died of diphtheria, Kiss found evidence of considerable myocardial damage and he believed that the large volume of antitoxin and blood serum given intravenously might have contributed to the cardiac failure.

In cases of *heart failure*, **ouabain** given intravenously seemed to prevent cardiac dilatation, in the experience of E Lesné and B Zadoc-Kahn (Rev franç de pédiat 9 454, 1933). By use of the electrocardiogram, they found 11 patients of a group of 100 who had abnormalities of cardiac rhythm, 34 with an unusual ventricular complex. A total of 5 per cent of patients with severe diphtheria, and 18 per cent of patients with mild diphtheria developed cardiac lesions. *Digitalis* was considered to be a *dangerous* drug for such patients and they advised that it be used cautiously, if at all.

Two instances of *laryngeal stenosis* in diphtheria patients were reported by J G Strachan (Canad M A J 29:404 (Oct ) 1933) who believed that the condition was caused by too frequent intubation. In both patients **tracheotomy** was subsequently done and the trachea dilated. The wound closed and the patients had no difficulty in breathing and speaking except for a slight amount of hoarseness. F. Barber (*loc cit*) reported a lower mortality rate from the use of tracheotomy rather than intubation.

Among other authors, there is no unanimity of opinion in regard to the better method of treatment of laryngeal diphtheria. Dangers accompany both procedures and the operator's skill and his judgment in individual instances seem to be the most important factor.

**Prevention.—Schick Test.**—Criticism of the value of the Schick reaction as an indication of the individual's immunity to diphtheria has arisen because of the incidence of the disease among those who had received active immunization. Although the negative Schick reaction is usually considered to be an indication of the immunity of a patient to clinical diphtheria, occasional exceptions were noted by P. Feuille, P. Thiry and C. Blancardi (Compt. rend. Soc. de biol. 115:367, 1934). They found previous reports in which as many as 1 per cent. of patients with negative reactions had contracted the disease. The explanations for this occurrence have been (1) the occurrence of other infections of the throats of patients who were diphtheria carriers. The general course of the disease and its response to antitoxin treatment should prove the diagnosis in such cases. (2) Errors in performing the Schick test and interpreting the reactions were thought to be unlikely explanations, because most physicians are inclined to interpret the doubtful reactions as positive rather than negative. (3) The skin test may not always indicate the minimum amount of  $\frac{1}{30}$  the unit of antitoxin and may be negative when smaller amounts of antitoxin are present in the blood. (4) During the course of certain intercurrent diseases the individual's immunity to diphtheria may decrease and render him temporarily susceptible to the disease.

With the idea that considerable fluctuation of the antitoxin content of the blood occurred under certain circumstances, the authors retested 246 soldiers who had negative reactions when they first came on duty. After a month of severe training, which produced a considerable amount of fatigue, 17 of these men or 6.91 per cent. of the group had positive reactions. It was concluded that this finding was no reflection on the value of the Schick test, but indicated the possibility of fluctuation of the blood content of immune bodies in any individual.

A group of 72 patients who developed diphtheria after receiving immunization treatment were reported by J. C. Saunders (Irish J. M. Sc 95:611 (Nov.) 1933). These patients constituted about 1 per cent. of the entire number treated (8027). In 33 instances the clinical diagnosis of the disease was not confirmed at the hospital and in 18 instances immunization had not been completed. Of a group of 27 patients who had received the total amount of treatment and sufficient time had elapsed for them to have developed their immunity, 13 had doubtful evidence of the infection, 12 others had not had Schick tests performed after the immunization treatment. Signs of clinical diphtheria were observed in 7 patients who were known to have had negative Schick reactions but the diagnosis was doubtful in 5 instances. The course of the disease was mild in all the patients who had received the immunization treatment with one exception of a slight cardiac complication.

In the opinion of G. Ramon and M. Djourichitch (Compt. rend. Soc. de biol. 113 996, 1933), the *immunizing power* of various lots of toxoid may vary

They injected 36 guinea-pigs with diphtheria toxoid and determined the antitoxin content of the blood in one-half of the number after 21 days and in the other half after 26 days. The animals were then inoculated subcutaneously with various amounts of a culture of diphtheria organisms. There were variations of response of these animals. Some of them with 20 units of antitoxin in their blood serum survived large injections, while others with the same antitoxin titer succumbed to smaller doses. The antitoxin in the blood, therefore, did not always indicate the degree of resistance to the infection.

A suggestion was made by E. Lorenz (*Ztschr. f. Kinderh* 55:282 (July) 1933) that the tissues rather than the blood hold the antitoxin and the negative Schick reaction indicates that there is a neutralizing amount of antitoxin in the skin of the patient rather than in the blood. He investigated the influence of injections of ordinary horse serum on the Schick reactions and on the antitoxin content of the blood in nonimmune children. After the administration of this serum to a group of 80 Schick-positive children, 1 to 14 years of age, 69 per cent. had subsequent skin tests which were either weakened or suppressed. This was much more marked in the younger age groups. The amount of influence depended upon the quantity of the serum injected per unit of body weight and upon the time between the serum injection and the subsequent Schick test. It has been noted that ordinary horse serum, which does not contain the specific properties of diphtheria serum, seemed to be a valuable aid in therapy when it was administered with diphtheria antitoxin. After injections of ordinary horse serum, the antitoxin titer in the blood was not increased, but 2 instances were cited in which children whose Schick tests changed from positive to negative as a result of these nonspecific serum injections and yet developed clinical diphtheria 8 to 14 days later.

Small quantities of blood or convalescent serum injected into Schick-positive individuals have been observed to reverse the skin reaction within 24 hours, according to H. E. Thelander (*J. Pediat* 4:75 (Jan.) 1934). Four to 6 c.c. of blood from an immune donor were given intramuscularly to each of 6 Schick-positive patients. The next day Schick tests were repeated and 4 were negative and 2 had reactions of smaller size. Seven children with positive tests were given blood transfusions and 4 had a reversal of the skin reaction, while 3 had smaller reactions. Although the Schick reaction was made negative, the antitoxin content of the blood did not rise to the standard quantities thought necessary to produce immunity except in 2 instances.

Other nonspecific factors which may influence the skin reaction have been discussed in relation to the Schick reaction of newborn infants. Recent studies by A. Rothholz and A. G. Kuttner (*Am. J. Dis. Child* 47:559 (Mar.) 1934) have confirmed the fact that the test in such patients is not a reliable index of the antitoxin content of their blood. A group of 100 mothers with positive Schick reactions had infants who had negative Schick tests in all but 6 instances. The explanation of this difference in reaction of mothers and their infants was sought in the differences in skin structure of infants and adults. Histologic examination of the skin of infants showed that the epidermal layers were relatively thicker and the papillae of the corium were less well defined than those of adults. This

difference was thought to account for the frequently imperfect placement of the test material in superficial layers of an infant's skin. On the other hand, it was thought possible that the infant's skin might be able to neutralize toxin *in situ* even though the antitoxin content of its blood was low.

The removal of tonsils and adenoids in Schick-positive patients has been reported to effect a change of the skin reaction in many instances. The results of these observations have been questioned by several clinicians. A controlled experiment of this kind was recently carried out by W. H. Park, C. Kereszturi and D. Hauptman (*Ibid.*, p. 565). Two groups of children living in congested urban districts were followed for a period of 6 months. One group of 46 children with positive Schick reactions had their tonsils removed and 6 months later 18 per cent. had developed negative reactions. Another group of 47 children with positive skin tests and living in the same city district did not have their tonsils removed and at the end of 6 months 21 per cent. had developed negative reactions. None of the children of either group had had clinical diphtheria or injections of a diphtheria immunizing material within the previous 6 months. There were about an equal number of diphtheria carriers in each group.

It has also been suggested that the effect of tonsillectomy on the production of immunity to diphtheria was greater among the urban population than among the rural one. In a rural community in the state of Washington, W. A. Buice (*Lancet* 1:790 (Apr. 14) 1934) found no significant difference in the percentages of positive Schick reactions of 110 tonsillectomized children and 122 with their tonsils intact, and there was little variation of the percentage of positive Schick reactions in different age groups. Clinical diphtheria was a rare disease in this community, only 7 cases occurring within the last 8 years. The removal of tonsils in such rural groups seemed to have little or no influence in immunizing children against diphtheria.

*Passive Immunization*—Passive immunization against diphtheria is often required by groups of susceptible patients in hospitals or other institutions. The amount of antitoxin necessary to produce the immunity and the length of time such protection remains was discussed recently by E. G. Munro Jones and J. D. Kershaw (*Brit. M. J.* 2:969 (Nov. 25) 1933). Among patients with scarlet fever who were exposed to diphtheria on a hospital ward, 100 had positive Schick reactions and were given 500 units of antitoxin. A total of 89 were immune for a period of 14 days. After 21 days, 91 were retested and 84 were still immune. No further tests were made, but it was thought improbable that the immunity lasted much more than 3 weeks. In regard to age, the authors noted that all of the children under 10 years were protected by the antitoxin but children over 15 years and adults generally seemed to require more than 500 units of antitoxin to insure immunity for the 3-weeks period.

*Active Immunization*—The last few years have witnessed rapid changes in the *type of material* used in producing active immunity. **Toxin-antitoxin** mixtures are being used less frequently. **Toxoid**, prepared by the addition of formalin to diphtheria toxin, is still a very popular immunizing agent in the United States and recently clinicians have been using **alum treated toxoid** with success. The relative merits of diphtheria toxoid and of alum treated toxoid

were compared in a study of several groups of children by J. L. White and E. A. Schlageter (J. A. M. A. 102:915 (Mar 24) 1934). Eight groups of 200 to 300 children each were given the immunizing material. Two injections of alum toxoid given in doses of 1 c.c. each, at intervals of 1 week, seemed to be more effective in producing immunity than similar doses of regular toxoid and the interval of 1 week between the two injections seemed to be as effective and harmless as the customary 3-weeks interval. Three doses of 0.5 c.c. alum toxoid given at weekly intervals was somewhat less effective than the 2 doses of 1.0 c.c. each. Single doses of either alum toxoid or ordinary nonalum toxoid were much less effective in producing immunity than 2 or 3 doses.

**Alum treated toxoid** was found to be the most suitable preparation for immunization against diphtheria by J. D. Monroe, V. K. Volk and W. H. Park (Am J. Pub. Health 24:342 (Apr) 1934) because of the higher degree of immunity produced within a shorter time. Reactions were obtained rather frequently with this material, but they were usually localized and of short duration. Moderate general reactions were observed in 7 per cent. of a group of 315 children. Two doses of 1.0 c.c. of the alum toxoid were recommended, although 3 doses were considered to give the most complete protection.

A single dose of **alum treated diphtheria toxoid** was found by J. N. Baker and D. G. Gill (*Ibid* 24:22 (Jan) 1934) to be effective in the immunization of children. Everyone of a group of 197 Schick-positive children were made negative by a single injection of 1.0 c.c. of the precipitated toxoid. A group of 1414 children who had not been Schick tested before treatment, received 1.0 c.c. of the alum toxoid and 97 per cent. were found to be negative 2 to 3 months later. Reactions were not severe as a rule, although 8 patients of a group of 16,289 (0.05 per cent.) developed local abscesses at the site of injection of the toxoid.

Good results with the use of **alum precipitated toxoid** in the immunization of children and adults against diphtheria were obtained by F. J. Kenny (Northwest Med 33:136 (Apr) 1934). Among a group of 215 susceptible patients, 1 to 35 years of age, 99 per cent. were made Schick-negative 7 weeks after the injection of a single dose of alum toxoid. The reactions, even in the older children and adults, were mild.

Many methods for the concentration and purification of **diphtheria toxoid** other than the alum treatment have been attempted during the last year. A. Wadsworth, J. J. Quigley and G. R. Sickles (J. Immunol. 25:139 (Aug) 1933) reported their method of **purification** of diphtheria toxoid **with** the use of **acetone**. Addition of this material precipitated the toxoid solution and the excess formalin, 60 per cent. of the nitrogenous material and 99 per cent. of the phosphorus were removed. The final product was a powder which was stable and could readily be standardized.

Employing a 1 per cent. solution of formalin added to the toxin and incubated at 36° C., the authors noted that detoxification was complete at the end of 4 days without any loss of the antigenic power of the mixture. After 10 days' incubation a definite reduction in the antigenic properties of the toxoid occurred. Flocculation with toxoid purified with acetone occurred in the same manner as

with standard solutions of toxoid but the time required for the reaction was prolonged.

T. Spasowicz and W. Porebski (Compt. rend. Soc. de biol. 113:1267, 1933) used **benzoic acid** to concentrate **diphtheria toxoid** material. The benzoic acid dissolved in acetone was added to a cold aqueous solution of diphtheria toxoid and the benzoic acid was immediately precipitated, carrying with it the active principle of the toxoid. Removal of the benzoic acid left a white powder which was redissolved in physiologic saline solution. The nitrogen content of the toxoid mixture was greatly reduced by this procedure.

In consideration of the increasing number of reports of purification of diphtheria toxoid, certain requirements of any practical method were established by G. F. Leonard and A. Holm (J. Infect. Dis. 53:376 (Nov.-Dec.) 1933): (1) The method should not be too complicated, and (2) it should give a satisfactory yield; (3) at least half of the foreign protein should be eliminated; (4) the purified toxin should respond to the flocculation test, (5) sterilization by filtration should be possible, (6) the material should be stable for at least a year; and (7) the antigenic properties should be superior to those of the crude toxoid.

In experiments of their own, the authors employed ammonium sulphate, methyl alcohol, ethyl alcohol, acetone, acetic acid, hydrochloric acid, acid and alcohol precipitation, aluminum hydroxide, potassium alum and sodium alum. The method which met the above requirements best was the precipitation of the crude **toxoid** with **ammonium sulphate**, subsequent dialysis and precipitation with **acetone** and **alum**. According to flocculation tests with antitoxin, the highest yields of antigen were obtained by this method.

Mixtures of ordinary **toxoid with sterile hydrous wool fat** were made by H. W. Straus (J. A. M. A. 101:192 (July 15) 1933). One c.c. of the material contained 100 flocculating units. A single intramuscular injection of 0.2 c.c. to 0.25 c.c. of this toxoid in 103 susceptible individuals resulted in negative Schick tests in 99 per cent. of the group within a period of 2 months. The majority became immune at the end of 6 weeks after the injection. The reactions consisted of mild local tenderness and redness in all the children except one who developed slight systemic symptoms for 24 hours. Among 5 adult patients, 2 had rather severe generalized reactions. It was thought that this method of immunization was especially practical during epidemics. The hydrous wool fat apparently delayed the absorption and elimination of the toxoid which accounted for the high percentage of patients obtaining immunity.

The *size of the dose* of ordinary toxoid and the *frequency of its administration* has been questioned for several years. The possibility of a variation in the strength of commercial diphtheria toxoids has been suggested by W. Levin and H. A. Cary (Am. J. Pub. Health 23:1067 (Oct.) 1933). Employing such tests as the Ramon flocculation reaction, guinea-pig inoculation, and human experiment, these investigators found differences in potency in 5 different commercial brands of toxoid. Since individual tests often varied in their measurement of the antigenic properties of toxoid, a combination of experiments was strongly advised. In a group of 352 susceptible children who received 2 toxoid injections

of 1 c.c. each at 3-week intervals, the percentages of immune patients at the end of 3 months varied from 82 to 100 per cent., depending upon the sample of toxoid used. According to the authors, these variations make the necessity of a subsequent Schick test in all children especially essential in order to assure protection from the disease.

Very small doses of concentrated toxoid, injected intradermally, were employed by A. Goldbloom and D. L. Klein (*J. Pediat* 3:112 (July) 1933) to produce active immunization. Of a group of 12 Schick-positive children, 9 were given intradermal injections of 0.1 c.c. of the material and 3 received 0.2 c.c. Four became Schick-negative within 6 weeks, and 1 at the end of 3 months. Antitoxin in the blood of these children measured  $\frac{1}{25}$  to  $\frac{1}{10}$  units. Another group of 5 susceptible children received 0.2 c.c. of the concentrated toxoid intradermally in a single dose. Four of these were Schick negative at the end of 14 days. The fifth child was given another intradermal injection 2 weeks later and became negative after 7 days. One child had a severe local and general reaction.

Since the Schick test itself may have aided in stimulating the formation of antitoxin in the blood of the above patients, another group of 10 children were selected who had not had skin tests previously, but whose blood antitoxin was found to be below the immunity level. Six children were given a single intradermal injection of 0.2 c.c. of the toxoid, 4 developed sufficient antitoxin in their blood within 2 weeks to 2 months to give them protection. Four other children with low blood antitoxin levels developed sufficient antitoxin within 11 to 25 days after 2 injections of 0.2 c.c. One child received 0.4 c.c. of the concentrate (equivalent to 2.0 c.c. of normal diphtheria toxoid). He developed immunity within 1 month. Patients who had marked local or general reactions to the intradermal injections developed immunity in much greater numbers than did those who reacted weakly or not at all. Individuals with moderately high antitoxin titer in their blood before treatment were very easily immunized, while others with very little blood antitoxin at the start were much more difficult to immunize.

The immunization of adults, especially nurses and doctors who are Schick-positive, is a difficult matter because of the frequency of severe reactions encountered. The problem was successfully met by A. E. Keller and S. Harris (*J. A. M. A.* 102:2163 (June 30) 1934) by employing preliminary skin tests with the toxoid material and the use of diluted material in the sensitive individuals. Those with positive Schick tests were given intradermal injections of 0.1 c.c. of a 1 to 10 dilution of the ordinary diphtheria toxoid. If the local area of redness was not greater than 0.5 inches in  $\frac{1}{2}$  hour, regular undiluted toxoid was administered in doses of 0.3 c.c., 0.5 c.c. and 1.0 c.c. at intervals of 3 weeks. If the reaction to the skin test was greater than the above, diluted toxoid (1 to 10) was given in an initial dose of 0.2 c.c., and at each subsequent injection the dosage was doubled until the required amount was given. As a rule, the reactions were mild, but if severe reactions occurred, the dosage was reduced. By this method of treatment, negative Schick reactions were obtained in all of a group of 72 physicians and nurses.

The necessity of performing a Schick test on patients who have received immunization treatment is illustrated by the observations of J. Greengard (*Am. J. Dis. Child.* 47:799 (Apr.) 1934). In a group of 63 patients tested at intervals after toxoid treatment, 11 had reversal of their skin reactions from negative to positive. Ten of this group were less than 6 months of age at the time they were treated. Of a group of 214 susceptible children under 2 years of age, 14 infants did not develop negative Schick reactions after 2 injections of the diphtheria toxoid. Of this group of 14 children, 13 were less than 6 months of age at the time of the immunization. Young infants seemed to develop antitoxin slowly and in small quantities. Patients who developed immunity rapidly apparently retained it longer.

The rôle of the private physician in the campaigns of mass immunization of children and the relation of his work to that of the Public Health Clinic was discussed recently by G. W. Anderson and G. H. Bigelow (*Am. J. Pub. Health* 23 655 (July) 1933). A comparison was made between the activity of clinics in certain cities and the distribution of ampoules of the toxin-antitoxin to private physicians. Variable factors entered into the interpretation of the statistics, such as the economic condition of the community and the actual use of the ampoules which were given the physicians, but such consistent results occurred in the different localities in which campaigns were conducted that the following conclusions were considered justifiable: As a rule, the more active the immunization work was in the clinics, the greater was the demand by the private physicians for the ampoules and the more numerous the request for treatment by the inhabitants of the community. Conversely, the absence of an active clinic campaign in a community resulted in very little demand of the people for such treatment by their physicians. The incidence of diphtheria was found generally to be smaller in communities where active immunization campaigns had been conducted.

**DIPHTHERIA CARRIERS.**—The part played by cats as carriers of diphtheria bacilli and as possible agents disseminating the disease among children was suggested by E. B. Brooks (*Am. J. Dis. Child.* 46 1338 (Dec.) 1933). Schick tests performed on 70 cats and kittens were negative in every instance and the animals seemed to be very resistant to injections of toxin. About 5 times the minimal lethal dose for guinea-pigs was necessary to kill kittens. Diphtheria bacilli planted on the scarified mucous membranes of the noses and throats of these animals lived only 24 hours, but if other organisms, such as those of Vincent's angina, were present in the same locality, the diphtheria organisms survived for 4 days. On the fur of cats, the diphtheria bacilli lived for 3 days. It was concluded that (1) cats might act as carriers of the bacilli by contamination of the fur; (2) the animals were generally not susceptible to the infection of the nose and throat, but might harbor the microorganisms for a short time, especially when other infections such as Vincent's angina coexisted.

It is apparently possible for a diphtheria carrier to infect himself in some unusual part of the body. Two such patients with diphtheritic skin infections were described by H. Lausecker (*Munchen med. Wchnschr.* 81:213 (Feb. 9) 1934). Both harbored the bacilli in their nasal secretions and were Schick-



positive One developed an ulceration of a vaccination pustule and the other an ulceration of rhagades about the mouth, both lesions having the characteristic appearance of diphtheria lesions and containing the microorganism

**Treatment.**—The treatment of diphtheria carriers with disinfectants has not been successful, according to the survey made by A. Landou (*Acta pædiat.* 15:211 (Mar. 23) 1934). In certain instances, specific surgical treatment seemed to be effective. Patients who harbored the bacilli in the *throat* were usually cured by the complete **removal of their tonsils**. In 9 patients treated in this manner, the bacilli disappeared When the microorganisms persisted in the *nose*, there was usually found to be some abnormality of structure or some chronic disease. In 4 instances, **drainage of the sinuses** caused a disappearance of the bacilli and in 1 patient the **removal of a foreign body** resulted in a cure; in a third, the treatment of an atrophic rhinitis by **nasal irrigations** freed the patient from diphtheria organisms. No contraindications for such operations were noted by the author, although he recommended that a prophylactic dose of **antitoxin** be given the patient immediately before such treatment

### HEART DISEASE IN CHILDREN.—CONGENITAL LESIONS.

—One of the most common congenital heart lesions is *patency of the interventricular septum* In a group of 100 children with congenital heart lesions observed by D. C. Mur and J. W. Brown (*Arch. Dis. Childhood* 9:27 (Feb.) 1934), 40 had defects of the interventricular septum only The chief criterion for the diagnosis was a loud systolic murmur heard best in the third and fourth interspaces near the sternum Of the total group of 40, there was a preponderance of females, 25 in all Two children were Mongolian idiots and in a third the xiphisternum was missing The great majority of the entire group of patients had no symptoms of cardiac disease Two had been cyanotic at birth, 1 had palpitation, and 1 had dyspnea on exertion Cyanosis had occurred in 5 patients, but in only 2 children had it been an important symptom No constant disturbances of nutrition were noted, nor was there any characteristic x-ray shadow, and only 12 of the group had globular-shaped hearts No instances of heart block were noted in this series

*Congenital heart block* is a comparatively rare condition and sometimes it seems to be caused by defects in the septum L. M. Blackford and H. M. McGehee (*Am. Heart J.* 9:96 (Oct.) 1933) discovered congenital heart block in a patient 19 years of age who had an unusually slow heart rate On further investigation it was found that there had been a slow fetal heart rate and a persistently slow rate throughout life One short attack of syncope had occurred at the age of 9 years When 10 years of age, the patient had had a pulse rate of 44, rising to 56 on exertion At the age of 19 years the electrocardiogram showed an auricular rate of 65, a ventricular rate of 54, and complete dissociation between auricle and ventricle The patient's activity was somewhat limited but, in general, his health was excellent. No evidence of other disease could be found to account for this heart condition

Two instances of this same condition were observed recently by D. B. Witt (*Am. J. Dis. Child.* 47:380 (Feb.) 1934) In one infant a bradycardia was noted 2 months before birth and the dissociation of the auricles and ventricles

was proved by an electrocardiogram 2 days after birth. The infant died 2½ months later and at autopsy a coarctation of the aorta was discovered but there was no defect of the interventricular septum. A second patient with the same condition was 6 years of age when the diagnosis was made.

A careful pathologic study of a case of *congenital heart block* was made by W. M. Yater, W. G. Leaman and V. H. Cornell (J. A. M. A. 102:1660 (May 19) 1934). Their patient was an infant, 18 hours old, who was intensely cyanotic, had a loud systolic murmur audible over the entire chest and a heart rate of 40 per minute. The infant died within a few hours and at autopsy the interauricular septum was found to be entirely absent and there was a defect in the membranous portion of the interventricular septum. Serial sections through the heart showed a well developed bundle of His and left bundle branch, but there was a separation of the auriculoventricular bundle from the auriculoventricular node and the right bundle branch was absent.

Eight other patients with *congenital heart block* were reported by M. Campbell and S. S. Suzman (Am. Heart J. 9:304 (Feb.) 1934) and 3 by L. Hays (J. Pediat. 4:380 (Mar.) 1934). The incidence of this condition is very low, but Campbell and Suzman (*loc. cit.*) believed it to be more common than the reported case histories indicated. They found 30 previous case reports of this type of block and listed the characteristic symptoms as a slow pulse rate at early age, an absence of a history of previous infection, occasionally the occurrence of attacks of syncope, and signs of congenital morbus caeruleus. Hays (*loc. cit.*) found previous reports of 39 such cases and he added the occasional finding of a loud systolic murmur and a short diastolic murmur over the midcardiac region, suggesting the presence of a patent interventricular septum.

In regard to *treatment*, **atropine sulphate** has occasionally been used with some success, but Leaman (*loc. cit.*) found it of no value in his patient and Witt (*loc. cit.*) observed that it retarded briefly the auricular contraction rate, and later accelerated both the auricular and ventricular rates but the block persisted. Campbell and Suzman (*loc. cit.*) found very little effect of atropine on the restoration of the normal auriculoventricular association.

Observations on the course and prognosis of patients with *coarctation of the aorta* have been the subject of recent reports. In a study of the cardiac output in a patient with coarctation of the aorta, A. Grollman and J. P. Ferrigan (Arch. Int. Med. 53:35 (Jan.) 1934) found that there was an increase which was within the upper limits of normal and resembled that of patients with hyperthyroidism. Basal metabolic determinations were also higher in this patient than in the average and the authors suspected that an increased supply of blood to the thyroid gland might account for its hyperactivity.

*Coarctation of the aorta* with ulceration and perforation was observed by F. C. Narr and E. T. Johnson (Am. J. Dis. Child. 47:91 (Jan.) 1934). Their patient, a boy 7 years of age, had a thick inflammatory exudate of the pericardium and a narrowing of the aorta at about the site of the ductus arteriosus. There were 2 ulcerations in the wall of the aorta and a perforation in one. From the ulcers and from the blood a streptococcus was isolated. A similar congenital lesion with dilatation of the aorta and subsequent rupture occurred in a patient

of H L. Stewart and S. Bellet (Am Heart J. 9:533 (Apr.) 1934). Death occurred at the age of 26 years and at autopsy, dilatation of the aorta proximal to the coarctation was observed, with a dissecting aneurism of the ascending aorta, together with cardiac hypertrophy and subaortic stenosis. The arterioles of the heart were thickened and it was thought this condition might have resulted from a hypertension above the place of coarctation, although some previous reports have indicated that thickening of arteries beyond the point of constriction was as marked as of those below it.

Causes of death in other reported cases of coarctation of the aorta were found to be spontaneous rupture of the aorta or heart in 40 instances, cerebral lesions, usually hemorrhage, in 24, cardiac decompensation in 60, and undetermined causes in 17.

Various rare congenital anomalies of the heart which have been observed recently include that reported by G R Murphy and L F Bleyer (Am J Dis Child 46:350 (Aug) 1933), who found an *atresia of the tricuspid orifice* in an infant 4 months of age. This was the fifteenth case of this kind on record. M Jacobi and A Heinrich (Am J. M. Sc. 186:364 (Sept) 1933) reported an instance of a congenital *communication between the aorta and right ventricle* in a child 1½ years of age, which was the fourth case of such an anomaly reported. A patient with *pulmonary arteritis and sclerosis, together with a defect of the interventricular septum, dextroposition of the aorta, and dilatation of the pulmonary artery* was described by H L Stewart and B L Crawford (Am J Path 9:637 (Sept) 1933). The unusual feature of this case was the fact that the patient lived to the age of 60 years with no signs of heart trouble until immediately before death. Two instances of *stenosis of the pulmonary conus* at the lower bulbar orifice with the interventricular septum closed occurred in patients of W W Eakin and M. E. Abbott (Am J M Sc 186:860 (Dec) 1933). Only 2 other instances of this anomaly were found to have been reported previously. A *trilocular heart*, consisting of 2 ventricles and 1 auricle and a patent interventricular septum, was found at the autopsy of an infant 15 months of age by E Jaso and P Bernal Fandos (Arch de méd d enf 36:736 (Dec) 1933).

Two unusually early *diagnoses of congenital heart lesions* were reported by A L Dippel (Am J Obst and Gynec 27:120 (Jan) 1934). In 1 instance, the diagnosis was made before the child was born, because of the irregular rhythm and the loud systolic murmur heard in the fetal heart. Shortly after the baby was born, cyanosis developed and death occurred 60 hours later. Postmortem examination showed a transposition of the great vessels, a large patent foramen ovale, a rudimentary tricuspid valve, a small patency of the interventricular septum and small hemangiomas on the mitral valve. The ductus arteriosus was patent and the pulmonary valve was stenotic. The other infant had a fetal heart rate of 50 during the time of its delivery. It died 87 hours later and at autopsy there was found a stenosis of the isthmus of the aorta, a patent foramen ovale and interventricular septum, a patent ductus arteriosus, a liver which had central necrosis with chronic passive congestion, and lungs spotted with hemorrhagic areas.

Many patients with congenital heart malformations succumb to superimposed infections at the sites of the defects. More unusual is the triple lesions of *congenital heart disease with a superimposed rheumatic infection and bacterial endocarditis* observed recently by S. D. Leader and M. A. Kugel (J. Pediat. 4:595 (May) 1934). The patient first developed cyanosis at the age of 2 years. The following year she began to have recurrent attacks of joint pains and she died at the age of 12. At autopsy there were discovered a patent interventricular septum, stenosis of the pulmonary valve, dextroposition of the aorta, and stenosis of the right ventricle. The etiology of the stenosis of the pulmonary valve was thought to be inflammatory or rheumatic in origin and the subacute bacterial endocarditis probably was the terminal lesion.

**RHEUMATIC FEVER.**—*Etiology.*—*Predisposing Factors.*—Although the age at which the onset of rheumatic fever symptoms is most frequent is 7 or 8 years, there are occasional reports of the infection in very young children and infants. An instance of intrauterine rheumatic heart disease was reported by R. W. Kissane and R. A. Koons (Arch. Int. Med. 52:905 (Dec.) 1933). The mother had had frequent attacks of rheumatic fever and had a cardiac lesion and during her pregnancy she had several attacks of swollen painful joints and fever. At birth, the patient had red, painful, swollen joints and abnormal heart sounds suggesting some cardiac abnormality. Heart disease continued until the age of 9 years, when death occurred. Autopsy showed lesions characteristic of rheumatic fever in the myocardium and scars on the valves. The right auricle was much enlarged. Only 4 previous case reports of such an early infection had appeared in the medical literature previously. Three of the mothers had rheumatic fever during pregnancy and the fourth about 3 days after the birth of the child. One infant developed rheumatic fever 11 days after birth, one 30 hours after birth, one 3 days after birth and the fourth had the symptoms at birth. In none of these infants did cardiac damage occur.

Other predisposing factors of rheumatic fever, such as *climate, race, sex, diet, housing conditions* and other *infections*, have received a great deal of attention during the last year. J. S. Davis (Am. J. M. Sc. 186:180 (Aug.) 1933) made a statistical study of the incidence of rheumatic fever since 1898 in 2 of the New York City hospitals. Wide fluctuations occurred from year to year in the number of patients admitted with this disease, but a general decrease occurred both in absolute and in relative numbers compared with other diseases up to the year 1919. Since that time there has been a gradual increase. Carditis, on the other hand, occurred more frequently up to 1919 and was noted less often since that time.

In searching for explanations of the variation in incidence of the disease, the authors were unable to find any etiologic relationship of the foci of infection, especially infected teeth and tonsils.

The possibility of cyclic variations in virulence of the disease was mentioned as a possible factor since there was a steady decline of deaths from the rheumatic fever syndrome which was quite parallel to that of scarlet fever and other streptococcal diseases.

There was a greater incidence of rheumatic fever during the more rainy years, but these statistics, together with contradictory reports elsewhere, left doubt in regard to the etiologic importance of rainfall.

The effects of poverty, inadequate diet, insufficient clothing and other economic factors, as determined by the commodity retail price averages, in relation to yearly incidence of rheumatic fever did not seem to have any direct correlation.

There seemed to be no doubt of the low incidence of rheumatic fever in the warmer, southern parts of the United States. Rheumatic heart disease is not common in Florida, according to the report of E. S. Nichol (*Am. Heart J.* 9: 63 (Oct.) 1933). Among 16,200 medical patients in Miami, Florida, only 16 were cases of rheumatic fever. The author observed 413 patients with organic heart disease in private and clinic practice, but only a fourth of this group (103) had had rheumatic fever symptoms, and only 6 of this number had contracted the illness in southern Florida. Rheumatic heart disease among school children occurred 3 times more frequently among those who were born in the north and had moved to the south, than among those who were born in Miami. Patients with rheumatic heart disease who moved from northern climates to Florida seemed to improve rapidly.

On examination of hospital and clinic records of 8530 children, 3 to 14 years of age, who were living in Florida, only 2 instances of rheumatic endocarditis were discovered, an incidence rate of 0.035 per cent. According to the investigators E. W. Bitzer and G. L. Cook (*South. M. J.* 27: 503 (June) 1934), only 2 patients with acute rheumatic endocarditis had been seen in 25 years of private practice in that State.

In a review of 200 patients with rheumatic fever manifestations living in the Piedmont areas of Virginia, A. D. Hart, J. E. Wood and A. D. Daughton (*Am. J. M. Sc.* 187: 352 (Mar.) 1934) reported an incidence of 1.35 per cent among the total number of medical and pediatric admissions during a 6-year period. Among adult medical patients admitted to the hospital, 1.54 per cent were suffering from rheumatic fever. This was a higher rate of incidence than that observed in certain tidewater areas of the State, but was about the same as that reported from a Baltimore hospital, and was lower than the incidence of the disease in Boston. Rheumatic fever manifestations were somewhat more frequent among females than males and more common in the white than in the negro race. Of the entire group of 200, only 158 had joint pains, 11 had chorea only, and 21 had valvular lesions only. Valvular disease of the heart occurred in 138 or 69 per cent of the entire group, mitral lesions being more than twice as frequent as those of the aorta.

A summary of certain epidemiologic and clinical aspects of a group of 458 children with rheumatic fever who had been observed in Philadelphia over a period of 10 years was given by W. D. Stroud, M. A. Goldsmith, D. S. Polk and F. Q. Thorp (*J. A. M. A.* 101: 502 (Aug. 12) 1933) as follows: (1) The average age of the patients when the first symptom of the disease was noted was 7.3 years. (2) Of 307 children whose records were adequate and available, 40.7 per cent. were dead or totally disabled and 59.3 per cent. were able to work or go to school. (3) The best prophylactic treatment seemed to be the prevention

of colds and other respiratory infections. (4) The bulk of the primary manifestations of the disease occurred between December and May, with the peak in March. (5) Racial incidence occurred in order of greatest frequency in children of Italian, Hebrew, American and Irish parents. (6) Familial incidence was high. (7) The removal of tonsils and the proper treatment of sinuses seemed justifiable in this type of patient. (8) Of the irregularities of rhythm, premature contractions were rare and auricular fibrillation, when present, was usually a late or terminal manifestation. (9) The virulence of the infection, the resistance of the individual and the number of recurrences of the infection were more important factors in prognosis than were the number or extent of the valvular lesions. (10) Treatment of cardiac patients in a convalescent home was thought to be beneficial to the patient.

The influence of *puberty* on the recurrence of polyarthritis has been noted frequently. A few observations made by E. von Eickstedt (Ztschr. f. Kinderh. 56 64 (Feb ) 1934) confirm this opinion. Of a total number of 86 children with polyarthritis before the advent of puberty, 38 could be followed until after the changes of puberty had definitely taken place. Periods of about 4 years before and 4 years after puberty were compared. In the first period, 11 relapses and 16 recurrences occurred in the 38 patients. After puberty 1 relapse and 1 recurrence was noted. In contrast to tuberculosis, which often becomes more severe and active during puberty, acute polyarthritis apparently is favorably influenced by sex maturation.

Other investigations in regard to the etiology of rheumatic fever have resulted in the establishing of a relationship between pathologic findings in *scurvy* and *rheumatic* infections. J. F. Rinehart, E. L. Connor and S. R. Mettier (J Exper Med 59·97 (Jan ) 1934) noted that guinea-pigs with scurvy and a hemolytic streptococcus infection develop degenerative and proliferative lesions in the heart valves and myocardium which are not unlike the pathologic changes found in rheumatic fever patients. The animals were fed a diet deficient in vitamin C for 22 days and then injected in the right thigh with 0.1 cc of a hemolytic streptococcus culture. The joints of these animals became swollen and sometimes stiffened. In chronic scurvy the synovia was found to be covered by a fibrinous hyaline material and some areas of hemorrhage were noted. In one animal a subcutaneous nodule developed. Both of these lesions resembled those of rheumatic fever patients. Occasionally these changes occurred in animals with chronic scurvy only, but were much more evident in those who had superimposed infections with the hemolytic streptococci.

Among the infections which immediately predispose to rheumatic infections, *scarlet fever* has been especially interesting because of many similarities between the two diseases. In order to determine the relationship between postscarlatinal arthritis, rheumatic fever and carditis, J. R. Paul, R. Salinger and B. Zugar (J Clin Investigation 13 503 (May) 1934) investigated the familial incidence of rheumatic fever symptoms in groups of such patients. A high incidence of rheumatic symptoms were found to have occurred in families of patients with postscarlatinal arthritis and carditis. Rheumatic fever manifestations occurred in 4.3 per cent. of control families, in 12 per cent. of families of patients with

scarlet fever, in 10 per cent. of families of patients with rheumatic fever and in 35.8 per cent. of the families in which a member had had postscarlatinal arthritis or cardiac damage.

The relationship between *tuberculosis* and certain polyarthritic pains has been discussed recently by A. Raschewskaja, D Piskarew and W Ljachowsky (Beitr z. Klin. d. Tuberk. 84:177 (Dec. 23) 1933). They report 3 such instances which they have observed, but they were unwilling to consider tuberculosis the etiologic agent unless certain criteria were fulfilled, such as (1) the absence of other infections, (2) an acute exacerbation of the tuberculous infection, (3) the failure to respond to salicylates, (4) absence of cardiac lesions, (5) and possibly the presence of a positive tuberculin reaction.

Several clinicians have noticed an immediate response of an old rheumatic infection to *serum injections*. Two instances were observed by J Huber (Bull Soc. de pédiat de Paris 31:451 (Nov.) 1933) in which the injection of diphtheria antitoxin was followed by an exacerbation of rheumatic carditis. One patient, 13 years of age, developed urticaria and joint pains 12 days after the serum injection and the other child, 7 years old, developed the same symptoms 15 days after the injection. Both had severe exacerbations of the cardiac disease and the former patient died. In the opinion of the author, the nonspecific serum might possibly have been the cause of the lighting up of the rheumatic infection.

In another patient observed by J Huber (*Ibid* 31:500 (Dec.) 1933), joint pains and a heart murmur developed shortly after an injection of antitetanus serum. This patient had had no previous attacks of rheumatic fever and the lesion produced in the heart disappeared after several months. The author thought that the possibility of a coincidental rheumatic infection in this instance was unlikely. However, he believed that the necessary administration of serum to a rheumatic patient should be accompanied by salicylate therapy to prevent the exacerbation of a carditis.

**Bacteriology.**—A search for specific etiologic agents of rheumatic fever was made recently by H J Gibson and W A R Thomson (Edinburgh M J 40:93 (June) 1933). Cultures were made of the throat secretions of 200 patients with rheumatic fever and 242 normal control patients. *Streptococcus viridans* occurred in all cultures of both groups. *Hemolytic streptococci* were found in about an equal number of patients of both groups. Intradermal tests with saline suspensions of ground bacteria of hemolytic, viridans and gamma strains of streptococci showed very little difference in the percentage of positive reactions between the two groups, although more of the rheumatic group of patients (68.1 per cent.) had strong reactions than of the control group (55.4 per cent.). To Dick toxin, 81 per cent. of the rheumatic patients were negative as compared to 74.2 per cent. of the control patients. Fewer rheumatic fever patients who were febrile gave positive reactions to skin tests with hemolytic streptococcus extracts than nonfebrile and chorea patients. Positive skin reactions were more frequent in rheumatic patients with normal throats than in control patients, although hemolytic streptococci were recovered in a few more instances from the latter patients.

Of the rheumatic patients, 13 per cent. had had scarlet fever previously, but positive skin reactions to hemolytic streptococci were found in percentages quite similar to that of other patients who had not had the disease previously. In 5 instances, the rheumatic manifestations had followed closely after the attack of scarlet fever.

The authors concluded that the hemolytic streptococcus may play some part in preparing the way for rheumatic infections, but that probably some toxin or virus or possibly an allergic reaction was itself responsible for the disease.

An extensive study of the types of bacteria occurring in the throats of rheumatic fever patients was made by I. Weinstein and N. C. Styron (Arch. Int. Med. 53: 453 (Mar) 1934) and they were unable to find any direct relationship between throat infections and rheumatic symptoms. Of the group of 321 patients studied, slightly less than half were suffering from rheumatic fever and the remainder were normal individuals or those suffering from other illness who served as a control group. Hemolytic streptococci were found as frequently and in equal abundance in the two groups. In patients suffering from colds and sore throats, hemolytic streptococci were found as frequently in the control group as in the rheumatic patients. Rheumatic patients with their tonsils removed did not have these streptococci as frequently as those who still had tonsils. Green producing streptococci and indifferent streptococci were found in almost all the patients. Exacerbations of the rheumatic fever symptoms occurred as often among well rheumatic patients as among those with throat infections, but the majority of those who had exacerbations did have hemolytic streptococci in their throats. The authors concluded that these microorganisms might have an etiologic relationship to the rheumatic fever.

The presence of antistreptolysin in the blood sera of patients with rheumatic fever was demonstrated by W K Myers and C S Keefer (J Clin Investigation 13: 155 (Jan) 1934). In a group of 220 patients the content of antistreptolysin of the blood of those with streptococcus infections was compared with that of normal individuals. Higher titers of this substance occurred in those with rheumatic fever, scarlet fever, erysipelas and tonsillitis than in normal patients or in those with rheumatoid arthritis or other types of joint diseases. No relationship between streptococcus antitoxin and antistreptolysin could be discovered.

**Diagnosis.**—Early diagnosis and the determination of the activity of rheumatic symptoms is important and quite often very difficult. The differentiation of various muscle and joint pains was studied over a period of years by M. Seham and E. H. Hilbert (Am J Dis Child 46: 826 (Oct) 1933). They found no evidence that muscle pains were a result of normal growth and believed that the term "growing pains" should be discarded. Chronic fatigue and certain orthopedic conditions such as flat feet and scoliosis were often noted as the cause of chronic muscular pain, but if neither of these conditions was present, some chronic infection was usually the etiologic factor. Of the group of 208 children between 8 and 15 years of age, 21 per cent. had muscular pains for a period of 3 months or more. There was a definite relationship between inadequate sleep, fatigue and the occurrence of these muscle pains. When the muscle pain did not occur in any relationship to fatigue or in definite locality in the body, but did develop at certain



seasons and following infections such as sore throat, the pain was considered to have an infectious background. Elevated sedimentation rates, increased streptococcus agglutination titers, and increased incidence of valvular heart disease in such a group of children gave further proof of an infectious, probably rheumatic, origin of these muscular pains.

Methods of determination of the state of activity of a rheumatic infection include the *leukocyte count*, the *sleeping pulse rate* in comparison with the waking pulse rate, the *fever*, *weight gain* and *sedimentation rates*. Employing these tests R. R. Struthers and H. L. Bacal (Canad. M. A. J. 29:470 (Nov.) 1933) observed that chorea patients who had not developed any cardiac lesion usually had no elevation of temperature, no increase of the number of leukocytes above normal, a normal sedimentation rate, a marked variation in the sleeping and waking pulse rates and they usually gained weight when the proper treatment was given. When chorea was accompanied by heart disease there was frequently no increase in the leukocytic count or temperature, but the patients ceased to gain weight and the sleeping pulse rate was more rapid than normal. Patients with joint pains and associated cardiac lesions usually had elevated temperatures, leukocytosis, a failure to gain weight and abnormal sleeping pulse rates. The sedimentation rates in both conditions were increased and tended to remain so for several months thereafter. In cardiac decompensation they reached very low levels. The sedimentation rate was thought to be the most delicate test of all.

In a review of 360 children with rheumatic heart disease, observed in an ambulatory clinic and private practice, J. B. Wolffe (Arch. Pediat. 50:832 (Dec.) 1933) concluded that there were certain criteria by which the activity of the disease could be determined. These were: (1) the history of joint or muscle pain, (2) frequent gastric upsets and abdominal cramps, (3) repeated attacks of pharyngitis and tonsillitis, (4) involuntary twitchings, (5) enuresis after earlier bladder control, (6) cardiac pain, and (7) general lack of vitality. Physical findings indicating activity of the disease were: (1) a pale appearance, found in 30 per cent of such children, due usually to low hemoglobin values, (2) an overactive heart, (3) frequent elevations of temperature, (4) infected throats, (5) abnormal cardiac signs, such as friction rubs, enlargement of the heart, failure of the patient to gain weight, endocardial lesions, (6) occasionally an elevated leukocyte count and, sometimes, (7) electrocardiographic evidence of heart damage.

The *sedimentation test* was employed in children with rheumatic disease by H. W. Elghammer (Arch. Pediat. 51:281 (May) 1934) to measure the degree of activity of the infection. A group of 171 children were followed over a period of 10 months with the Landau modification of the micromethod of sedimentation. Five to 14 tests were made on each patient. The sedimentation rate seemed to indicate minimal activity of rheumatic disease better than any clinical sign or the temperature records. Uncomplicated chorea did not change the normal sedimentation rate, but associated rheumatic nodules, respiratory infections and endocarditis caused an increase in the rate and the convalescence could be followed closely with the subsequent tests. The removal of tonsils in rheumatic patients produced a temporary increase in the sedimentation rate and in one instance in which

endocarditis followed, the high rate persisted. In 4 patients with persistently high rates, the prognosis was observed to be unfavorable. Three of these patients subsequently died and the fourth was in a serious condition.

Alterations in the *blood* of patients with acute rheumatic fever were noted by V. V. Pezharskaya (Sovet. vrach. gaz. p. 771 (May 31) 1934; J. A. M. A. 103:382 (Aug. 4) 1934). A mild hypochromic anemia occurred in early uncomplicated cases and a more severe anemia in patients with recurrent attacks or with complications.

In acute stages of the disease the leukocytes increased in number as the temperature increased above normal; there was a diminution of eosinophils, and usually a shift to the left of the neutrophils. When complications occurred, the leukocytosis preceded the rise in temperature; there was often a relative neutrophilia and lymphocytopenia and often an eosinophilia and a monocytosis. During convalescence, the lymphocytes returned in relative proportions to as high as 50 per cent. and often an eosinophilia developed. Sedimentation rates gave a more accurate indication of impending exacerbations than did the leukocyte count. The author suggested that a pronounced anemia or marked leukocytosis at the onset of a rheumatic infection indicated either the presence of a complication or another superimposed infection.

**Complications.**—Widespread pathologic lesions throughout the entire body in patients with rheumatic disease have been described frequently. Within the last few years, especial attention has been paid to changes in the vascular system. Lesions in 164 patients who died of *embolic manifestations* of rheumatic heart disease during a period of 25 years were described by S. Weiss and D. Davis (Am Heart J 9:45 (Oct) 1933). Infarctions were found in one or more organs in 73 patients, or 45 per cent. of the group. These lesions were found in the lungs most often and, in order of frequency, in the brain, kidneys, spleen, arteries of the legs, mesenteric and iliac arteries and the aorta. In 34 patients, or 21 per cent. of the group, embolism was an important factor in causing death. Auricular fibrillation occurred in 74 patients, or 57 per cent. of the group, and this irregularity seemed to bear a more definite relationship to the formation of mural thrombi than did the activity of the rheumatic infection. The source of the emboli was determined in only 30 instances and the failure to find the source in other cases was thought to be due to either the complete dislodgment of the original thrombus or to the fact that the small verrucous vegetations were the cause of the embolic manifestations.

Certain clinical observations were of interest. The visceral emboli, which have been previously considered to be the cause of an immediate sharp pain, seemed, instead, to cause a slow dull pain which increased within a few minutes to a few hours to a severe pain. Embolism in the arteries of the extremities sometimes caused a coldness, tingling or numbness of the part affected rather than severe pain. Early recognition of this condition is important because surgical removal usually gives good results if attempted within a few hours after the onset of the attack.

Related to this condition is the *hemorrhagic eruption of the mucous membranes of the mouth and pharynx* in patients with rheumatic fever which has been

observed by E. Holtz and G. Friedman (Am. J. M. Sc. 187: 359 (Mar.) 1934). A group of very small deep red spots occurred most frequently on the buccal mucous membranes near the orifice of Stensen's duct and were seen also on the soft palate, fauces, uvula, tips and borders of the tongue and on the tonsils. This eruption was observed in 13 of a group of 19 patients with rheumatic heart disease and in only 1 instance among a group of 29 patients with other illnesses. The enanthem was noted occasionally in certain patients with related rheumatic infections such as erythema nodosum, tonsillitis, rheumatoid arthritis, acute upper respiratory infections, subacute bacterial endocarditis and congenital heart disease with unexplained fever. Although the histologic sections of this eruption indicated the presence of hemorrhage, an increased vascularity of the region and a thickening of the media and intima of the vessel walls, there were no typical Aschoff lesions.

A rather rare complication of acute rheumatic fever is *thrombophlebitis*. C. Bruce Perry, O. C. M. Davis and B. Schlesinger (Lancet 2 966 (Oct 28) 1933) described 3 such cases in patients 11, 20 and 13 years of age, respectively. The thrombosis followed phlebitis and since the histologic findings in one case resembled those of rheumatic lesions elsewhere, it was concluded that the virus of the disease might have attacked the wall of blood-vessels, producing clinical symptoms of pain which were followed by thrombosis and the swelling of the part of the body affected.

The pathologic changes occurring in the *coronary arteries* of patients with rheumatic fever were noted recently by H. T. Karsner and F. Bayless (Am. Heart J 9 557 (June) 1934). The studies were made of 56 hearts of autopsied patients who had had definite clinical evidence of rheumatic fever. Each decade of life was represented by this group of patients. As a control, 40 hearts of non-rheumatic patients were examined. Rheumatic fever constantly produced lesions of the coronary arteries of inflammatory or fibrotic character, but similar pathologic changes could be produced by other infections. Aschoff's nodules were characteristic of rheumatic fever only. The distribution of the lesions throughout the coronary vessels was irregular and the relationship to myocardial disease could not be ascertained, although late myocardial fibrosis was greater than might be expected from early acute myocarditis alone.

In early life, rheumatic fever seemed to predispose to fibrosis of the coronary arteries. The sequence of the lesions of the blood-vessels resembled that which occurred in the endocardium and pericardium.

*Aortitis* in children is a rare condition but such cases have been observed by B. H. Neiman (J. Lab. and Clin. Med. 19: 929 (June) 1934), together with a similar lesion in a young adult 27 years old. These lesions were characterized by verrucæ in the aorta and streptococci were present in one instance. The lesions in the intima resembled rheumatic nodules found elsewhere in the body. The verrucæ seemed to begin formation with fibrinoid swelling at the point of attack of the invading body and later became necrotic and infiltrated with fibroblasts. In one instance an aneurism developed and ruptured into the pericardial sac. One child, 11 years of age, had a stenosis of the isthmus of the aorta, with verrucæ formation and spontaneous rupture of the aorta.

In the opinion of M. Pomerance and S. Frucht (Am. J. Dis. Child. 47:1087 (May) 1934), every cardiac irregularity occurring during an attack of rheumatic fever is to be considered as a form of *heart block* which may be detected by electrocardiograms. Often these lesions are very transitory in nature and are probably due either to edema surrounding an Aschoff's body situated in the conduction bundles, which might interfere with the blood supply of that area, or possibly to some toxic factor which acts as an irritant to the cardiac muscle, causing certain independent rhythms which that portion of the heart assumes occasionally. The author reported 3 cases of rheumatic fever, one of which had electrocardiographic evidence of left bundle branch block, another, a complete heart block and the third an auriculoventricular dissociation.

**Prognosis.**—The relationship of active rheumatic fever to the course of heart disease was determined from the clinical records and autopsy findings in 161 patients of all ages by M. A. Rothschild, M. A. Kugel and L. Gross (Am Heart J 9:586 (June) 1934). As evidence of activity were the presence of Aschoff bodies in 95 instances and fibrinous pericarditis, verrucous endocarditis, acute myocarditis or auricular lesions in 11 other instances. There were 55 patients with old valvular deformities and occasionally old auricular lesions, but with no Aschoff bodies or fibrinous pericarditis. These were considered to be quiescent cases. From a comparison of these 2 groups of patients, it was concluded that circulatory failure in the first 5 decades of life usually resulted from active rheumatic infections and that considerable mechanical defect within the heart did not in itself justify a poor prognosis.

In a review of the cause of death in a group of 148 patients with rheumatic heart disease, C L. Laws and S A Levine (Am J M. Sc. 186 833 (Dec) 1933) found that congestive heart failure was responsible for only 33.1 per cent of the deaths. Other causes were acute rheumatic carditis in 23 per cent, peripheral emboli or thromboses in 11.5 per cent, subacute bacterial endocarditis in 29 per cent, and other cardiovascular diseases, such as angina pectoris, pulmonary edema and the like, in 3.4 per cent. of the cases. The oldest patients died with congestive failure, the youngest, with acute rheumatic carditis. Patients with aortic disease only were the oldest at the time of death (average age 52.5 years), those with mitral disease only were next in age (42.8 years), and those with multiple lesions were the youngest (30 to 35 years). Deaths were twice as frequent in females as in males in the group of cases of acute rheumatic carditis and the opposite ratio was characteristic of those with thrombi or emboli. Auricular fibrillation occurred most frequently in patients with mitral stenosis, with congestive heart failure or with emboli, and was much less common in other types of rheumatic cardiovascular disease.

An investigation of the cause of death of 100 patients with mitral stenosis was made from the clinical and pathologic findings by C S Stone and H S Feil (Am Heart J 9 53 (Oct) 1933). It was noted that 56.6 per cent of the group had had a history of rheumatic fever. The majority of the patients were females and of the white race and the average age of the males at time of death was 42.7 years, 4 years greater than that of the females (38.6). Auricular fibrillation occurred in 53 per cent. of the patients and was usually associated with intra-

cardiac thrombi and emboli. Fibrillation did not occur in 5 patients with subacute bacterial endocarditis. Cardiac disability occurred in 87 patients, circulatory failure in 81, subacute bacterial endocarditis in 5, acute bacterial endocarditis in 1, and acute verrucose endocarditis was present in 48 cases. Mitral stenosis occurred as the only lesion in 54 patients and was associated with other valve lesions in the remaining 46.

**Treatment.**—Treatment of rheumatic fever in children with intravenous injections of **streptococcus vaccine** seemed to have very little beneficial effects, according to the report of M. G. Wilson, M. G. Joseph and D. M. Lang (Am J. Dis Child. 46:1329 (Dec.) 1933). Of a group of 166 patients, about half of the number received the hemolytic streptococcus vaccine and the remainder who were not treated served as a control group. These groups were observed for 3 years. Of another group of 141 patients, 89 were treated with various other antigens and the remainder were not. These were observed for 2 years. The antigens employed in the latter series were typhoid vaccine, polyvalent streptococcus vaccine and streptococcus viridans vaccine. Mild reactions occurred in 21 patients.

There was very little difference in the frequency of recurrences during the 3-year period in the group treated with hemolytic streptococcus vaccine and those not treated. The occurrence of exacerbations of the disease was 48 per cent in the first year, 39 per cent in the second year, and 37 per cent in the third, but those receiving 2 courses of treatment did not do as well as those who received only 1 course. Patients receiving typhoid vaccine had recurrences in about the same rates as the above. The other antigens had no apparent effect on the number of recurrences of the disease.

The injection of **aqueous extracts of streptococci cardioarthritides** has been tried by J. C. Small (J. Lab. and Clin. Med. 19:695 (Apr.) 1934) in the treatment of rheumatic carditis. A suspension of the streptococci in normal saline solutions in concentrations of about 100 million bacteria per c.c. was allowed to stand for 7 days in a refrigerator and then the bacteria were removed by filtration. Dilutions of  $10^{-14}$  to  $10^{-16}$  were employed. Following the injection of these extracts, a mild exacerbation of the symptoms occurred and usually 3 types of reaction were noticeable. The primary reaction developed in 24 to 48 hours and this was often followed by a feeling of euphoria and then a secondary reaction. Individuals differed in their response to such injections, but the optimum type of reaction seemed to be a very mild primary phase and a long euphoric stage. Adjustment of the dosage for each individual was directed towards this end, beginning with 0.05 c.c. of the  $10^{-16}$  dilution and repeating the dose every 5 to 7 days. The patient was observed for tachycardia, cardiac arrhythmia or mild rheumatic pains and the dosage was increased only in the absence of these symptoms. Evidence of improvement in the patient's general condition was an elevation of the erythrocyte count, leukocyte count, hemoglobin content, decreased sedimentation rate and increased opsonic index of the patient's serum for the streptococcus cardioarthritides. When improvement was noted in the patient after 6 to 8 injections, the time between treatments was lengthened.

to 10 to 14 days and later to 3 or 4 weeks. The individual dosage was rarely carried higher than 0.1 c.c. of  $10^{-14}$  dilution.

In the treatment of acute rheumatic fever *following tonsillitis*, A. Streubel (Med. Klin. 29:1106 (Aug. 11) 1933) reported some success with the application of **alcohol and spirit of tannin to the tonsils** 3 times a day. Intramuscular injections of 0.5 to 1.0 c.c. (8 to 16 minims) of a **turpentine** preparation every 3 or 4 days produced a counterirritation which seemed to relieve the attacks of joint pains.

For a child 10 years of age, who was suffering from advanced *mitral stenosis* and *auricular fibrillation*, S. J. Jenkins and N. Owens (Arch. Pediat 50:479 (July) 1933) reported favorable results from the use of **quinidine**. The first dose was 2 grains (0.13 Gm.), the second, 3 grains (0.2 Gm.) 3 times a day, and thereafter an increase of 3 grains (0.2 Gm.) a day until a total of 30 grains (2 Gm.) a day had been reached. After 164 grains (10.6 Gm.) had been administered the heart rate returned to normal, but the patient developed a rash. The drug was discontinued for a few days, then given in decreasing doses for a short time. For 5 months the patient was well but then began to fibrillate again. Quinidine sulphate was again given in divided doses of 6 to 15 grains (0.4 to 1 Gm.) a day. The fibrillation ceased temporarily but congestive failure developed soon afterwards. The drug was not well tolerated the second time and apparently had no lasting benefits.

**ENDOCARDITIS.**—In order to investigate the relationship between rheumatic fever and *subacute bacterial endocarditis*, O. Saphir and S. A. Wile (Am Heart J. 9:29 (Oct.) 1933) reviewed the clinical and pathological findings in 10 patients with the latter disease. Eight of these patients were children over 5 years of age and 2 were young adolescents 19 years of age. In every instance there was a clinical history of previous rheumatic infection, pathologic evidence of Aschoff's bodies in the myocardium besides healed endocarditis and subacute bacterial endocarditis, positive blood cultures of *Streptococcus viridans* and Gram-positive cocci on the heart valves.

Although the authors believed that it is possible that the two diseases could occur accidentally in the same patient or that an allergic state was responsible for the occurrence of the two infections, they thought it was most likely that the rheumatic fever produced such damage of the heart that the field was made favorable for the development of the bacterial endocarditis.

An unusual type of endocarditis occurring in 2 brothers was observed by J. Hallé and Derome (Bull. Soc. de pédiat. de Paris 32:237 (Apr.) 1934). The disease was characterized by a polymorphous erythema, arthritis and signs of endocarditis involving the aortic valve especially. A small coccus form of microorganism was isolated from the knee joint of one patient but could not be definitely identified. The disease was fatal in one of the 2 brothers.

An instance of *gonorrheal endocarditis* in an infant, 10 days old, following a gonorrheal conjunctivitis, was reported by W. W. Brandes (Am J Dis Child 46:341 (Aug.) 1933). The eye infection began when the baby was 3 days old and a smear showed Gram-negative diplococci, both intracellular and extracellular. At necropsy, vegetations on the tricuspid valve were found to contain

the same type of organisms. The ductus arteriosus was widely patent. According to the authors, this was the youngest patient with this type of endocarditis ever reported and the only one in which such a heart lesion secondary to conjunctivitis had been observed.

Two instances of *congenital endocardial* lesions, which apparently developed as a result of some inflammatory process, were described by G. Stohr (Arch. Path. 17: 311 (Mar.) 1934). One infant was 48 hours old, and the other 9 days of age at the time of death. Both had malformations of the left side of the heart and of the proximal portion of the aorta. Histologic examination showed an endocarditis with thickening of the endocardium and an extension of the process into the myocardium, and round cell infiltration in 1 instance. Areas of necrosis and calcification were found in the papillary muscles. The valves were generally free from involvement.

**IDIOPATHIC CARDIAC HYPERTROPHY.**—Considerable doubt has arisen during the last few years whether idiopathic hypertrophy of the heart is a clinical entity. F. E. Kenny and S. Sanes (J. Pediat. 3: 321 (Aug.) 1933) believe that many instances of so-called "idiopathic" hypertrophy of the heart in infancy have some definite bacteriologic or toxic background. They cite 2 cases of cardiac dilatation and hypertrophy which followed acute infections in infants 6 months and 1 year of age, respectively. At autopsy, no gross evidence of infection could be detected, but microscopic examination of the heart muscle showed parenchymatous changes in the muscle fibers with degeneration, vacuolation and round cell infiltration and necrosis. In 1 patient there was evidence of fibrosis together with hypertrophy of the remaining muscle fibers. In the author's opinion, the lesions in the heart of these patients began with degeneration and necrosis of heart muscle fibers due to the action of a toxin, possibly from bacteria. This was probably followed by an interstitial reaction, later by fibrosis and attempts at muscle regeneration and hypertrophy.

An instance of cardiac hypertrophy in an infant 16 months of age was observed by G. Blechmann, Deberdt and R. Azoulay (Arch. de méd. d. enf. 37: 154 (Mar.) 1934). The symptoms of heart disease began at the age of 11 months and slowly grew worse, with signs of cyanosis, dyspnea and tachycardia. At autopsy the heart was greatly enlarged partly due to dilation of the left side of the heart. No definite etiology could be determined.

**HEART IN OTHER DISEASES.**—Serial electrocardiograms of 8 children during attacks of *bronchopneumonia* were made by A. F. Abt and M. I. Vinneccour (Am. J. Dis. Child. 47: 737 (Apr.) 1934). These children were 4 months to 7 years of age and none received medication, such as digitalis, which might affect the cardiac muscle or the conduction. In 2 instances the P-R interval was prolonged, in 1 patient to as much as 0.24 second, and the T waves in  $L_1$  and  $L_3$  were smaller and less peaked during the acute illness in every case and were inverted in 1 instance. A right axis deviation occurred twice. Such changes were thought to be due to toxic myocardial lesions.

The effect of the *dysentery* group of diseases on the heart was studied in 9 children with electrocardiograms and autopsy findings by P. von Kiss and R. Martyn (Arch. f. Kinderh. 101: 67 (Jan.) 1934). Certain pathologic changes

were observed in the regions of the sinus node and in portions of the auricles and there was dilatation of the coronary vessels. Tachycardia, which was a prominent symptom in these patients, may have been due to these anatomic changes or may have been a functional disturbance. In the more chronic forms of the disease the heart was atrophic and resembled that of older persons. The possibility of insufficient nutrition of the heart muscle due to the tachycardia and absence of sufficient relaxation of the heart muscle was considered as one factor leading to exhaustion.

In 6 of the 9 patients, death occurred in 3 to 6 days after the onset of the infection. The pulse rate increased in the early stages to as high as 200 and the electrocardiograms showed a flattening and prolongation of the T waves and a change in the form of the S-T segments opposite to the characteristic changes of coronary occlusion. The tachycardia continued throughout the illness and the changes in the S-T segments became more pronounced. The T waves reached as high as the R waves. In the final moribund stage the rate decreased to 80 or 100 and the auricular conduction time became longer and more irregular and the T waves became diphasic. These changes were accentuated as the patient died, the bradycardia became more pronounced and the Q R S complex was prolonged. In the more prolonged illnesses, the electrocardiograms were like those of old patients, in that the R waves were low and split and the T waves flat.

**FUNCTIONAL HEART MURMURS IN CHILDREN.**—Many procedures for differentiating functional from organic heart murmurs have been devised but none have proved to be very satisfactory. A method recently described involves considerable apparatus and time. M. H. Bass, H. Mond, C. R. Meseloff and E. T. Oppenheimer (*J. A. M. A.* 101:17 (July 1) 1933) made heart sound tracings with a phonocardiograph of a group of 64 children with organic or functional murmurs. Systolic murmurs were found to be composed of vibration frequencies varying from 60 to 600 oscillations per second. All types of the murmurs recorded contained high vibration frequency components, but the presence of low vibration factors varied considerably. The latter were present in 75 per cent of patients with obvious organic heart disease and were absent in 86 per cent of patients thought to have normal hearts. It was hoped that this method of diagnosis might be an additional aid in differentiating functional from organic systolic murmurs in children.

The incidence of functional heart murmurs before and after exercise in a group of 275 boys, 5 to 18 years of age, was reported by W. J. Siemsen (*Am. J. Dis. Child.* 47:1100 (May) 1934). Only 9 per cent of the group had such murmurs during a quiet state, but they occurred in 46 per cent after exercise. A venous hum was audible at the base of the neck in 49 per cent of the group. Extrasystoles occurred in 3 boys and split heart sounds very frequently. All of these findings were considered to be inconsequential in respect to impairment of cardiac function.

**INFANT FEEDING.**—*In Newborn.*—That there may be some advantage in adding alkali to cow's milk dilutions when fed to newly born infants is suggested by the work of V. W. Lippard and E. Marples (*Am. J. Dis. Child.*



46·495 (Sept.) 1934). They found that the acid-base balance of the newly born infant was less stable than that of older infants and that daily ingestion of small amounts of alkali-producing salts brought about alterations in the acid-base balance of their blood. The authors were able to compensate the diminution in the alkali reserve in newborns produced by the ingestion of cow's milk, by the daily addition of approximately 0.25 Gm. (4 grains) of **sodium bicarbonate** to the formula. They observed greater increases in weight in infants who received sodium bicarbonate and **sodium citrate** in addition to cow's milk dilutions than in those who received similar formulas without added alkali.

**Artificial Feeding.**—In the chairman's address at the Section on Pediatrics of the California Medical Association, W. M. Happ (J. Pediat. 3:772 (Nov.) 1933) makes a plea for less stereotyped methods in infant feeding, particularly as far as quantity of feedings is concerned. He cites the marked variations in the amounts taken at breast feedings both by the same baby at different feedings during the 24-hour period and by different babies of the same weight and age for the total 24-hour period. Greater dependence should be placed on the satisfaction of the baby's appetite. Forced feeding should not be permitted even though the baby does not take the prescribed amount of the formula. On the other hand, if his appetite is not satisfied with the quantity prescribed, more should be given. By this method reasonable gains in weight should be obtained provided there is no other reason for failure of development.

An abbreviated and simplified infant feeding schedule is recommended by A. Tow (Arch. Pediat. 51:49 (Jan.) 1934). Simple dilutions of cow's milk with added sugar are given to artificially fed babies. Normal infants weighing over 5 pounds are fed at 4-hour intervals without a 2 A. M. feeding. As soon as possible, usually about the third month, the 10 P. M. feeding is omitted, so that the child is on a 4-hour feeding schedule. **Orange juice**, up to 2 ounces (60 c c) and 20 to 40 drops of **viosterol** were given daily. The **yolk of a coddled egg** is started at 3 months, **cereal** at 4 months, **vegetables** after the fifth month, and **meats** are added as soon as the child is placed on a 3-feeding schedule which occurs between the sixth and seventh months.

**Soft Curd Milk.**—A study of soft curd milk, including its production and characteristics as well as its value in infant feeding, has been carried on by M. Morris and G. A. Richardson (J. Pediat. 3:449 (Sept.) 1933). Contrary to the general impression that individual cows secrete milk of uniform curd tension, they found that a cow may secrete milk of varying curd tension throughout a single lactation period. In conformity with previous investigations, the milk of low curd tension was found to be low in nonfatty solids, notably in proteins. The investigators reported that, in line with this, the average milk of low curd tension was low in energy value, with a lower buffer capacity than that of milk of average composition. The rennin coagulation and pH as well as the bacterial flora showed no significant variation from the usual market milk. The curd tension of market milk was appreciably reduced by boiling for 3 minutes with comparatively little increased reduction after boiling for 10 minutes. Increased dilution of the mixture had a pronounced effect upon the lowering of the curd

tension. The already low curd tension of evaporated milk was not appreciably affected by boiling.

In a clinical study, the authors fed soft curd milk to a group of infants and compared the results with infants fed undiluted boiled certified milk and diluted evaporated milk formulas. They found that infants required more soft curd milk than ordinary cow's milk, probably because of the lower energy value of the soft curd milk.

It was their clinical impression that it was difficult to start an infant on soft curd milk; but when started, while it was not superior to other "accepted formulas," it was a satisfactory infant food and produced excellent tissue turgor.

They concluded, "considering (1) the variability in the production of soft curd milk and the increased observation necessary in its production; (2) the lack of superior results when used in comparison with other accepted infant formulas, soft curd milk does not warrant special production and certification for use in infant feeding."

**Mineral and Nitrogen Retention Studies.**—Further evidence of the adequacy of **evaporated milk** as a substitute for fresh cow's milk in infant feeding is given by P C Jeans and G. Stearns (Am. J. Dis. Child. 46:69 (July) 1933) They found that 9 healthy male infants made an excellent growth in length and weight when fed on a mixture of equal parts of evaporated milk and 12 per cent corn syrup, acidified with lactic acid. The periods of observation varied from 18 to 48 weeks Orange juice, cod-liver oil, egg yolk, fruits and vegetables were fed in addition at suitable ages. The retentions of nitrogen, calcium and phosphorus were high and were approximately the same as those which had been obtained when undiluted acidified fresh milk was fed to a group previously studied They interpret the high retention of nitrogen, high excretion of creatinine and good physical progress as evidences of good muscular growth Similarly, the high retention of calcium and phosphorus, early carpal ossification, rapid growth in body length and the absence of clinical or chemical evidence of rickets are considered evidences of good bone growth.

The effect of *varying sugar intake* on nitrogen, calcium and phosphorus retention of children has been studied by R. B. Hubbell and M. Koehne (*Ibid* 47:988 (May) 1934). Seventeen children from 7 to 11 years of age, who were already on a controlled diet for other metabolic studies, were used in this study. During the period of investigation the only variable factor in the diet was the sugar intake During an initial period of low sugar intake there was an average retention of nitrogen of 0.026 Gm, of calcium of 0.005 Gm, and of phosphorus of 0.007 Gm. per Kg per day, respectively. When sufficient sugar was added to the diet to increase the caloric value approximately 6 per cent, there was no change which could be attributed to the added sugar. The addition of sufficient sugar to increase the caloric value of the diet from 16 to 18 per cent. resulted in a tendency toward an increased retention of nitrogen and phosphorus The retention of calcium was somewhat decreased in 3 of 7 cases

It is rather commonly considered that one of the effects of **vegetable feeding** is increased retention of minerals That this is not the case when spinach is fed to young infants is stated by F. W. Schlutz, M. Morse and H. Oldham (*Ibid*

46.757 (Oct.) 1933). In their studies they found that the influence of spinach feeding on mineral retention was negligible in the case of the very young infant. In some instances they found, particularly in the case of calcium and iron, addition of spinach to the diet may lead consistently to slightly decreased retentions. In no case was such feeding followed by a consistent increase in retention. They suggest that any favorable effect produced by vegetable feeding to young infants must be attributed to vitamin content or other still unknown factors.

The excretion and retention of nitrogen, calcium and phosphorus of several **soy bean** preparations has been studied by G Stearns (*Ibid.* 46.7 (July) 1933). There was a relative increase in the intake of nitrogen and calcium as compared to the phosphorus intake. This resulted in an insufficient retention of phosphorus. The urinary excretion of calcium was markedly increased and that of phosphorus decreased. The substitution of dicalcium phosphate for calcium carbonate in the soy bean preparation improved the relative retention of nitrogen, calcium and phosphorus. The author believes this modified soy bean food to be a satisfactory food for infants when a milk substitute is needed, as in the treatment of certain allergic conditions.

**Cereal and Vegetables.**—In order to determine what advantage there might be, if any, in early feeding of solids to infants, M. M. Glazier (*J. Pediat.* 3.883 (Dec.) 1933) has started 4 different groups of infants on cereal, strained vegetables and fruits, egg yolk, toast and zwieback at varying age periods. Thus Group 1 was started on these foods in addition to the milk formula and cod-liver oil and orange juice during the second and third months of life, Group 2, during the fourth month; Group 3, during the fifth and sixth months, and Group 4, between the seventh and tenth months. From the results of his observations he concludes that better nutrition and better food and bowel habits were found in his first group in which solids were added in the second and third months of life. He believes that this is due to increased amounts of vitamins A, B, C, and D, iron to prevent nutritional anemia, increased bulk of stool, decreasing the tendency to constipation, and that earlier experience with solid food tends to prevent disturbing food habits at a later date.

The effect of cooking on the digestibility of cereals has been studied by J. R. Ross and L. M. Burrill (*Ibid.* 4.654 (May) 1934). No significant differences were found in the relative starch digestibility of Cream of Wheat, corn meal, Mead's Cereal, Quaker rolled oats and Quick Quaker oats. Whole wheat was slightly less readily digested. Cooking for more than 30 minutes in a double boiler did not significantly increase the digestibility of cereal starches, as evidenced by the amount of maltose and of total carbohydrate formed *in vitro* under standard digestive conditions. The starch digestibility of a special pre-cooked cereal mixture was found to be more rapid than the starch digestibility of any of the other cereals tested.

**Kraut Juice.**—Another method for making milk antirachitic as well as antiscorbutic has been suggested by C. V. Rice (*Arch. Pediat.* 51:390 (June) 1934). He has fed a number of infants whole milk or evaporated milk acidified with sauerkraut juice. No orange juice or cod-liver oil was given and the infants were not given sun baths. X-ray pictures of the wrists were taken at monthly intervals.

Only 3 of the infants developed rickets. Each of these had been given kraut juice from glass containers. Healing of the rickets followed substitution of kraut juice from tin containers. (Kraut juice loses its potency when kept in glass container.)

The method of preparing the milk is as follows. 1 quart of milk is boiled for 2 minutes and a sufficient amount of kraut juice is added to turn blue litmus paper red. Kraut juice may be added to evaporated milk in the same manner.

The author believes that the mineral and vitamin contents of sauerkraut juice are in all probability antirachitic and antiscorbutic. Certainly all infants who are fed in this manner should be checked for the presence of rickets with x-rays of the wrist taken at fairly frequent intervals.

**Rice Polishings.**—Vitamin B complex in the form of rice polishings has been added to a dried milk mixture and fed to 100 normal infants by M. F. Gaynor and R. H. Dennett (J. Pediat. 4: 507 (Apr.) 1934). In comparison with infants fed on a similar dried milk mixture without rice polishings, with infants fed evaporated milk and with infants fed modified cow's milk mixtures, these infants made a greater gain in weight. In addition anorexia and gastrointestinal disturbances were lacking, pallor was less marked and a greater resistance to infection was manifest.

**INFANT MORTALITY.**—The Birth and Death Registration Areas are now complete so that for the first time such data is available from every city of 10,000 population and over (Statistical Report of Infant Mortality for 1933; American Child Health Assoc. (July) 1934). The infant mortality rate in the 985 cities of the Birth Registration Area for 1933 is 57.1 per 1000 live births. While this figure is slightly higher than the 1932 rate of 56.8, the 1933 rate for only those cities included in the 1932 rate is 55.9. Thus, it may be safely assumed that there has been no real increase in the urban infant mortality rate during 1933.

In a general discussion on fetal and neonatal mortality C. G. Grulee (J. Pediat. 3: 132 (July) 1933) states that the chief hope of reducing the number of deaths in the newborn group lies in antenatal treatment of syphilis, in prevention of sepsis and in reduction of birth trauma. Little may be hoped for in the decrease of deaths due to malformations, congenital debility and allied conditions. He points out that present enthusiasm must not lead to expectation of a result comparable to the reduction of infant mortality in general. Further, while he acknowledges the part that bad obstetrics plays in producing birth injuries which result in death, he does not believe that all birth injuries may be ascribed to this cause and that a certain unknown percentage is the inevitable result of the birth process.

**MALNUTRITION IN CHILDREN.—Incidence.**—Whether there has been any increase of the number of malnourished individuals during the last few years of economic depression has been a question frequently discussed, and recent investigations, including that of E. Jacobs (Am. J. Pub. Health 23: 784 (Aug.) 1933) would indicate an affirmative answer. In a 5-year period from 1928 to 1932, from 1000 to 2000 patients were observed in a Community Health Center where the status of their nutrition was diagnosed on the basis of their

height, weight, condition of the skin and tissues, color of the mucous membranes, muscular development and tone, and their general physical condition. The diagnosis of malnutrition was made in 23 per cent. of the number of patients seen in 1928 and on 36.5 per cent of those seen in 1932. This increase was consistent throughout all age groups except the one covering the ages of 17 to 20 years. Other factors leading to malnutrition besides the lack of food may have been certain emotional disturbances such as worry.

The effect of the economic depression on the nutrition of school children of Pittsburgh was estimated from the records of weight, height and age which have been compiled for the last 10 years by A. M. Kerr (Pennsylvania M. J. 37:232 (Dec.) 1933). The Baldwin-Wood tables were used as the averages for making comparisons. In 1927 and 1928 there was an increase in the percentage of school children who were definitely underweight. It was believed that unemployment first became noticeable in those years. Within the next few years the percentage of markedly underweight children had increased from the usual level of 7 to 12.6. The number of children who were normal in weight, or above, dropped from 49.2 per cent. of the entire group in 1928 to 39.2 per cent in 1931 to 1932. Children of high school age seemed to have suffered from the effects of malnutrition most frequently. In the last year or two an examination of the pre-school children indicated that nutrition was improving in that age level. When milk was supplied in the schools, weight loss was checked in almost all children and satisfactory gains in weight were recorded.

Recent increases in mortality rates in Germany, especially during the months of February to May (Berlin Correspondence, J. A. M. A 101:1165 (Nov. 15) 1933) have been accredited in part to the deficiency of vitamins in the diets of many individuals of the lower social and economic classes and of the more rural districts. The decline in nutrition level has been thought to predispose these persons to tuberculosis and other infectious diseases.

**Etiology**—The factors influencing nutrition of children were summarized recently by W. R. P. Emerson (Arch Pediat 51:343 (June) 1934). The essentials for good nutrition and normal physical and mental development were considered to be: (1) freedom from physical defects, (2) adequate food, (3) free air, (4) sufficient exercise, and (5) proper rest. From a survey of a large number of children of preschool and school ages it was found that each child had an average of  $4\frac{1}{2}$  physical defects and 6 faulty eating habits. Of a group of 1000 children, only 2 per cent were found to be free from physical defects. The most frequent defects were those of nasopharyngeal obstruction, defective teeth, diseases of various organs of the body, and postural conditions which were either the result or a contributory cause of malnutrition. Among faulty health habits the author included the following:

I. Faults of control:

1. Removable physical defects uncorrected
2. Habits injurious to health.
3. Irregular habits of living
4. Uncontrolled likes and dislikes
5. Worry and fretfulness.

- II. Faults causing overfatigue:
  - 6 Irregular bedtime
  - 7. No regular rest periods.
  - 8. Overdoing at work and play.
  - 9 Eating when overtired.
  - 10. Inadequate vacations or weekly rest.
- III. Faulty food habits:
  - 11. Finicky about food.
  - 12. Habitual overeating or undereating.
  - 13. Fast eating or washing down food.
  - 14. Irregular mealtimes.
  - 15. Candy or sweets between meals
- IV. Faulty health habits:
  - 16. Working in poor air heated above 68° F.
  - 17. Sleeping with windows closed.
  - 18. Irregular time of bowel movement.
  - 19. Insufficient exercise or outdoor sunlight.
  - 20. Excessive tea, coffee or tobacco.

Sound nutrition seemed to lead to improvement of mental development, increased efficiency and increased resistance to disease.

In the author's opinion the present day health programs were placing too much emphasis on the diagnosis of disease rather than on the patient's health habits and daily activities.

Among the causes of undernutrition in infancy listed by B Schick and A. Topper (M. Clin. North America 17:1219 (Mar.) 1934) were: (1) Inherited constitutional inferiority, which may be exaggerated by poor hygiene and improper diets or by poor eating habits, (2) disturbances of digestion; (3) chronic infections. In later years the etiology may be overstimulation and emotional strain of school, extra curricular activities and fatigue.

Obesity in children usually results from: (1) overeating or underactivity or both; (2) disturbances of the internal gland secretions, especially of the thyroid, pituitary or gonads; (3) inherited constitutional tendencies

It was stated that the maintenance of normal nutrition depends upon (1) the basal metabolism of the patient, (2) the added energy consumed in muscular activity, (3) the energy required for the digestion of food, and (4) the energy necessary for growth and development. The caloric intake must meet the sum total of these requirements and a deficient diet will cause a loss of weight, an excessive diet will result in deposition of fat

The rôle played by *vitamins* in sustaining proper nutrition has been investigated from many angles. Recently, considerable attention has been given to vitamin A. A study of a group of 13 infants with evidence of vitamin A deficiency was made by K. D. Blackfan and S. B. Wolbach (J. Pediat. 3:679 (Nov.) 1933). The patients varied in age from 1 to 18 months, 8 were males and 5 were females. One patient, 1 month of age, had been breast-fed and had no clinical evidence of the disease but died of bronchopneumonia. Autopsy showed keratinization of some of the tissues and multiple abscesses in the lungs. In 6 patients the diagnosis of vitamin A deficiency was made before death by the occurrence of keratomalacia of the eyes. In 7 patients the diagnosis was established by

histologic examination of the tissues after death. Five of the last group had been diagnosed clinically as bronchopneumonia. One infant with clinical evidence of vitamin A deficiency survived but had a permanent injury of an eye.

In experimental animals it has been shown that deficiency of vitamin A caused an atrophy of epithelium and replacement with keratinizing stratified epithelium. In animals the involvement of the cornea of the eye was a late manifestation. Secondary effects of the avitaminosis were. (1) loss of weight, primarily of fat, but sometimes muscle tissue and that of other organs; (2) anemia; (3) cessation of bony growth; (4) degenerative changes of the skeletal muscles; and (5) lymphoid hypoplasia. In infants the epithelium of the trachea and bronchi was found to be attacked first and this may account for the prevalence of pneumonia in such patients.

Seven of the above series had received diets which were apparently adequate in vitamin A and it was supposed that other factors had interfered with the storage of this material. In one patient, congenital atresia of the bile duct was thought to have been a predisposing factor leading to avitaminosis. Since vitamin A deficiency may be a much more prevalent condition than previously thought and since the eye signs are comparatively late symptoms, the authors have suggested certain signs which might aid in the detection of the condition. They were (1) a careful history to detect any inadequacy of intake of vitamin A or its precursor, carotin, (2) the investigation of any chronic disease which might interfere with the metabolism of fats, such as vomiting, diarrhea, diseases of the liver, gall-bladder or pancreas, (3) the appearance of night blindness and xerosis of the cornea with opaque white deposits on the scleral conjunctivæ, (4) the demonstration of keratinized epithelial cells in the scrapings of the cornea, nose or mouth, and of the secretions of the trachea, bronchi, kidneys and vagina.

A review of the literature in regard to vitamin A deficiency in children was made recently by H. M. M. Mackay (*Arch. Dis. Childhood* 9: 65 (Apr.) 1934). The severe forms of this type of avitaminosis were found most frequently in India, China, the far East, certain parts of Central America and Labrador. Milder forms ordinarily unrecognized, were thought to occur in western Europe. Symptoms involving the eye have usually been observed in children whose diets were skimmed milk and carbohydrates chiefly, with a deficiency of meat, green vegetables, eggs and animal fats. The most common symptoms of vitamin A deficiency were found to be marasmus and keratomalacia. Changes occurred in epithelial tissue with extensive replacement of it with keratin. Early treatment with **cod-liver oil** will restore the child to a normal condition and prevent blindness.

An unusual nutritional disease of children associated with a maize diet has been noted recently in the Gold Coast Colony of Africa. A report of the condition observed in about 20 children was made by C. D. Williams (*Ibid.* 8: 423 (Dec.) 1933). The disease occurred in children 1 to 4 years of age and was characterized by edema, chiefly of the hands and feet, loss of weight, diarrhea, irritability, sores on the mucous membranes and desquamation of the skin. The symptoms developed slowly, the skin first becoming a dull reddish color and then black in patches on the ankles, knees, wrists and elbows, and gradually extending over the forearms, legs, thighs and buttocks. A few days later desquamation of

these areas left raw, pink areas. The skin at the corners of the mouth and eyes became involved and photophobia and corneal ulcers sometimes resulted. There was no evidence of anemia. Throughout these stages the diarrhea and irritability were severe, the pulse was rapid and the patients usually died if treatment was not given. The chief finding at autopsy was a pale, fatty liver.

The diets of all these infants consisted chiefly of breast milk and preparations of maize. There was no evidence of a deficiency of any of the vitamins unless possibly some part of the B complex. The symptoms did not resemble beriberi or pellagra. It was thought possible that some amino-acid or protein substance was missing in these diets. An adequate varied diet and especially a good grade of canned milk seemed to cure the disease.

The description of the symptoms and signs of this syndrome was thought by H. S. Stannus (*Ibid* 9:115 (Apr.) 1934) to resemble pellagra, which frequently occurs in persons on maize diets.

*Septic conditions* were considered by A. G. Ogilvie (*Ibid*. 8:413 (Dec.) 1933) to have definite effects on nutrition. In a group of 31 malnourished infants whose condition was not due to such predisposing factors as prematurity, tuberculosis and syphilis, the majority came from poor families and only 7 had been breast-fed longer than 10 days. The infections contracted by these infants were characterized by symptoms of a sudden onset of vomiting, diarrhea, rapid loss of weight, poor appetite and fretfulness. Occasionally a cough, dyspnea and pyuria occurred. The muscles became flabby and an anemia developed in which the hemoglobin fell to 50 to 70 per cent. This condition sometimes continued for weeks with frequent exacerbations, or it might suddenly subside, only to recur within a short time with some septic manifestation. There were 12 infants of the entire group who had these severe septic infections and 6 of them died after an average duration of 8 weeks of the illness.

The remainder of the group, 19 infants, had less acute attacks of illness, but the general course was somewhat the same. Repeated infections of the nose, throat and ears, loss of appetite, vomiting, diarrhea, and failure to gain weight were common symptoms. Well-balanced diets, antirachitic treatment and the administration of iron had no beneficial effects on the course of the disease, but it seemed that certain infants suddenly overcame the infection and recovered spontaneously. Six of the 19 infants of this latter group died.

Many of the cases of this sort were previously diagnosed as "feeding cases" but now it was thought that some infection was the basic cause. The portal of entry of the infection was thought to be the respiratory tract, but there was insufficient proof as yet. The prognosis depended upon the nutrition, weight and resistance of the patient, and upon the severity of the infection.

*Hydro-lability* is a term used by some investigators to designate an impaired function of tissues to retain water. The presence of this condition in malnourished infants was stated by J. C. Schippers (*Monatschr f Kinderh* 58:364 (July 27) 1933) to be the result of illness rather than to be the cause of it. The usual classification of the etiology of malnutrition has included 3 factors, alimentary, infectious and constitutional conditions. This last cause, that of constitutional disturbances, accounted for the smallest number of malnourished children of a



group of 691 reviewed by the author. Endogenous factors present at birth were responsible for malnutrition in about 25 per cent. of the group. Hydrolability was thought to be a serious manifestation of malnutrition and yet the underlying cause of this disturbance of nutritional state was often quite obscure.

**Diagnosis.**—In order to make a more accurate selection of malnourished children, R. Franzen (Am. J. Dis. Child. 47:789 (Apr) 1934) suggested the use of criteria which have empirical foundations of value. It was thought that any measurements of children should estimate the conditions of the muscles and subcutaneous tissues and should exclude individual skeletal differences. Various methods of measuring nutrition include: (1) the weight for height determinations, (2) the weight for height and width of hips, (3) the rating of the medical examiner, and (4) the so-called A. C. H. screen. This last method included measurements of arm girth (A), the chest depth (C), and the width of the hips (H). Simple computations made from these measurements give an index of nutrition. In a comparison of these different methods in a group of children 11 years of age, it was thought that the A. C. H. screen test gave much more accurate information of the state of the child's nutrition than did any of the other three.

Three general methods for estimating the nutrition of a child were described by Schick and Topper (*loc. cit.*) as (1) relationships between weight, height and age, (2) anthropometric measurements, and (3) the general appearance of the patient. Among the many tables and formulas employed in deriving indices of nutrition, they believed that the most accurate was the pelidisi index of Pirquet which made use of comparisons of the weight and sitting height of a child.

**Pathology.**—The manner in which *fat destruction* occurred in malnourished infants was described recently by H. Dorencourt (Nourrisson 21:221 (July) 1933). In the process of malnutrition the stored carbohydrates are utilized first, then the fat and last of all the protein. The disappearance of the fat deposits situated in various parts of the body follows a certain order, that of the abdominal wall disappearing first and then the subcutaneous layers of the chest, the back, and the loins. If the process continues, the fat of the arms, forearms, lower limbs and buttocks disappears in that order and last to go is the reserve fat supplies of the perivascular mesenteric regions and, finally, that of the face. Marfan has classified malnutrition according to the disappearance of the adipose tissue in these various localities. Even in the extreme degrees of marasmus, small islets of fat may be found in the thoracic and abdominal cavities and about the upper portion of the kidneys.

In the investigation of the reason for the definite order of disappearance of fat deposits, the author considered the possibility of variations of blood and lymph supply, muscular activity and differences in structure of the fat. The last factor was thought to be especially important. The body fats are composed of a mixture of 3 fatty acids, palmitic, stearic and oleic. The last one only is liquid at normal temperatures. Tests for the relative composition of these fats included determinations of the melting point, the iodine number, and the saponification index. The structure of fat was found to vary with different ages, and with different body locations. The melting point of fat is lower in the abdominal region than in the mesenteric or perirenal region and is higher in general in infants than in adults.

The iodine and saponification indices were lower for the fats of infants than for those of adults and were higher in abdominal regions than in the mesentery.

In this manner a study was made of the adipose tissue of 7 infants 6 weeks to 4 months of age, suffering with different degrees of athrepsia and the author found that the fat disappeared in an order depending upon the amount of unsaturated fatty acids (oleic) present. Adipose tissue containing the higher saturated fatty acids, such as palmitic and stearic, were more resistant to decomposition and destruction.

The relationship between *malnutrition* and *fatigue* and the *effects of muscular activity on certain body constituents* was investigated by F. W. Schlutz (Acta paediat. 16: 138, 1933). Various degrees of malnutrition were produced in dogs by treadmill exercises, swimming and different quantities of diet. The evidence of fatigue was much greater and the recovery from fatigue was much slower in the malnourished animals. Fatigue produced by swimming resulted in an increase of the sugar concentration and of the fixed acids in the blood serum. An initial rise in sugar and lactic acid occurring at the beginning of exercise often disappeared after continued muscular effort. When a state of exhaustion was reached the balance could no longer be maintained and the fixed acids developed to excess. Some malnourished animals who became exhausted by exercise had very low blood sugar levels, indicating that the fuel supplies of the body were insufficient to meet the demands of muscular activity.

**Treatment.**—The general treatment of undernutrition outlined by Schick and Topper (*loc. cit*) included: (1) a **concentrated high caloric intake**; (2) reduction of the basal metabolic rate by a **low protein diet**, a decrease in muscular activity by means of **rest periods** and **luminal**, if necessary; (3) **insulin** to stimulate the appetite. For reduction of body weight of the obese it was recommended that: (1) the **diet** be bulky and of lowered caloric value; (2) the metabolic rate be increased by a high protein intake, **increased muscular activity** and **thyroid extract** if the basal metabolic rate is low; and (3) the **salt and water intake** be limited.

**Insulin** has been employed in undernourished individuals who were not diabetic, to stimulate the appetite and to encourage gain in weight. L. S. Radwin and S. S. Brown (J. Pediat. 4: 315 (Mar.) 1934) gave 10 units of insulin twice a day to each of a group of 5 boys in an institution. They observed no unusual rate of weight gain as a result of this therapy. Another group of 5 boys received injections of 15 units twice a day and their weight gain was a little more rapid than that of a control series of 8 boys. One or 2 individuals in each group lost weight during the month of observation and there was no noticeable increase in the amount of food consumed by the insulin treated group. One child had a feeling of dizziness following most of the injections. After the insulin was discontinued, the patients who had gained weight rather rapidly, failed to continue to gain. The authors concluded that insulin treatment of undernutrition was not sufficiently successful to warrant its general use.

The addition of **soy bean flour** to the diets of children was found by G. W. Caldwell (M. J. and Rec. 138: 126 (Aug. 16) 1933) to improve nutrition. The soy bean has been used for many years as one of the chief constituents of the diet

by Chinese and Japanese and it seems to replace other proteins usually derived from meat and dairy products. It contains all the essential amino-acids, has a high mineral content, especially of phosphorus, and has large amounts of vitamins A and B. The author recommended that soy bean flour be prepared as a cereal, made into bread or added to milk. Of a group of 66 clinic patients of an average age of 27 years, each gained an average of 9.4 ounces a month over a period of 9 months. Of a control group of 50 children of approximately the same age, physical condition and economic status who received no soy bean flour, each gained only 6.7 ounces per month.

The simple regularity of **institutional care** in the treatment of undernourished children has been observed by H. L. Eder (*Arch. Pediat.* 50:628 (Sept.) 1933) to give excellent results. In his preventorium the children have a routine schedule for the day with a **sun bath** for an hour in the morning, a 2-hour **rest period** in the afternoon and 11 hours sleep at night. The diet was not unusual, except that it was well balanced and given regularly 3 times a day. **Cod-liver oil** and **orange juice** were given routinely and children who were anemic received an **iron tonic**. **Special exercises** for correction of *postural defects* were given regularly. The average gain in weight was 12½ pounds during the average stay of 22.6 weeks and the best and most permanent results were obtained in the children who were over 8 years old. The necessity of following these children at home after they had been discharged from the preventorium was thought to be important if any permanent benefits from the treatment were to be gained. Of 89 such children who were observed in outpatient clinics for an average period of 10.7 months after discharge from the preventorium, 94.5 per cent, had maintained good health.

The importance of **rest** in the treatment of undernourished children was stressed by R. A. Bier (*Ibid.* 50:527 (Aug.) 1933). For children in a Convalescent Home he found that added rest periods with an ordinary well-balanced diet resulted in considerable gain in weight. Of 117 undernourished patients, 58 reached normal averages of weight within a short time. Occasionally **cod-liver oil** and **maltine** preparations were added to the diet with good results.

The effect of **parental education** on the treatment of poor feeding habits of underweight and malnourished children was the object of an experiment conducted by C. T. Giblette and A. MacCrae (*Ment. Hyg.* 18:92 (Jan.) 1934). The work was carried out in a nursery school with supplementary cooking classes and instruction in child psychology for the parents and frequent visits to the homes. The group of children was composed of 25 boys and girls of a median age of 36 months, whose parents belonged to the lower social and economic levels. Of the group 23 had frequent respiratory infections, 18 suffered from constipation, 23 had irregular and insufficient hours of sleep, many had not established habits of feeding or dressing themselves and others had developed bad habits, such as temper tantrums, disobedience and the like. It was difficult to tabulate results from the educational program, but it was apparent that the great majority of children improved in their eating habits and general adjustment to their surroundings as the parents learned of the causes of their children's difficulties. Many of the faulty eating habits seemed to be accompanied by general

disorders of the child's behavior in the home and the child's desire for attention was often gratified by the parent's anxiety and over attention. As the intake of food declined, the child would become more irritable, sleep poorly, suffer from constipation and frequently develop respiratory infections. This undesirable chain of events could be broken by re-adjustment of home conditions and the education of parents so that desirable traits of the child's behavior were encouraged and the emotional background of social relations at home was stabilized.

**MENTAL DEFICIENCY IN CHILDREN.—Incidence.**—The incidence of mental deficiency in a community has always been difficult to determine. (Essays based on the Report of the Brock Committee, *Lancet* 1: 1011 (May 12) 1934.) In 1924, it was estimated that 8.6 per 1000 population in England were mentally defective and of every 100 such patients about 75 were feeble-minded, 20 were imbeciles and 5 were morons. The incidence was somewhat higher in rural communities than in cities. Variations in the criteria used in making the diagnosis of mental retardation have led to differences in figures obtained. In schools, about 15 to 30 per cent. of the children were found to be below the level of 75 in their intelligence quotients. There was also some evidence that the incidence of mental deficiency was increasing. If mental defects resulted from hereditary factors, and mating of mentally defectives occurred at random, only about one-tenth of the number of offspring should be defective. However, the figures indicated that mating did not occur at random and that the feeble-minded selected mates of similar intelligence, since at least one-third of the offspring were found to be defective. On the other hand, morons and imbeciles rarely have children and the feeble-minded have not been found to be unusually fertile.

It has been demonstrated mathematically by M. T. Macklin (*Canad. M. A. J.* 30: 190 (Feb.) 1934) that a continuation of a policy of nonelimination of the feeble-minded will tend to increase the percentages of such persons in any community, provided it is assumed that mental deficiency is primarily caused by hereditary factors. This would be especially true if the size of families of the mentally defectives continued to be larger than those of the normal or more intellectual persons. To prove that there has been an increase of incidence of the feeble-minded, the author cited the fact that during the last few decades the population of Canada had doubled while mental deficiency had increased 6½ times, too great an increase to be accounted for by improved methods of detection and better facilities for their care. Not only have the numbers of defectives increased in the last 60 years, but the rate of increase has been accelerating.

**Age of Walking as Related to Intelligence.**—According to Miles Murphy, of the Psychological Clinic of the University of Pennsylvania (*New York Times*, (Nov. 18) 1934), children with normal intelligence begin to walk at the average age of 15 months and those who are long retarded in walking "are significantly inferior."

The records of 712 children seen in the Clinic during a 5-year period were studied, and it was found that 350 of these were diagnosed as having normal intelligence and the remainder were feeble-minded. Records of the normal children, for whom the average age of walking was 14.99 months, revealed that

about 20 per cent of these started to walk before they were a year old, about 60 per cent when they were between 12 and 17 months and the remaining 20 per cent at 18 months. For the first of these three groups of normal children, the average intelligence quotient was 106, for the second group 110, and the third 93. "The superiority of group two over group one, in so far as their average intelligence quotients are concerned, appears to be a chance variation, but the difference between these two groups and the third group is sufficiently pronounced to be significant." In the records of the feeble-minded children, who were divided into 4 groups, according to the degree of their mental defect, there seemed to be definite evidence that the average age of walking increased as they passed from the milder to the more severe cases of defect. For the least defective group, the average age of walking was found to be 21.58 months, for the second group 25.05 months, for the third group 23.35 months, and for the lowest group, 32.17 months. The average for the feeble-minded was 86.65.

Although this study appears to have been entirely psychological in nature, and there is no reference made to the part played by any physical defect or neurological condition that may have been present in some of the children, and therefore related to the age at which the ability to walk was acquired, the observations are of sufficient clinical interest to bear further investigation.

**Etiology.**—*Heredity* has been considered to be one of the principal etiologic factors influencing the mental status of children. A great deal of difficulty has arisen in the investigation of the influence of these hereditary factors. The determination of mental retardation in family histories has been unreliable because of the lack of definition of minor antisocial tendencies or the degree of mental retardation necessary to be considered as feeble-mindedness, and the general difficulty in obtaining an accurate statement of the mental health of all of the members of a family (Essay based on the Report of the Brock Committee, *Lancet* 1:1121 (May 26) 1934). In a discussion of the methods by which mental defects are transmitted 2 theories were described. (1) Mental deficiency resulting from a single recessive Mendelian factor or gene seemed to occur in certain rare conditions, such as amaurotic family idiocy but not in the bulk of other types of mental retardation. (2) Damage to the gametes by certain toxic materials, such as those of alcohol, syphilis and tuberculosis, has been suggested as a possible cause of feeble-mindedness, but this theory has not been proved. There is definite evidence that x-ray and radium therapy can damage germ cells.

Mentally deficient parents have been found in only about 5 per cent of the groups of mentally deficient children, but the parents of 20 per cent were of low intelligence (*Ibid*, *Lancet* 1:1067 (May 19) 1934). The ratio of mental defectives to the probable "carriers" of mental deficiency was estimated to be about 1 in 10. On the other hand, a study of 3650 children born to parents of whom at least one was defective, revealed 1 per cent of superior intelligence and 40 per cent who were subnormal mentally. Environment, including prenatal factors, social conditions and parental influence, was also assumed to have a deleterious effect on the child's mental development.

The incidence of *positive Wassermann reactions* among mentally retarded individuals in 1.35 per cent. to 46.9 per cent. in the experience of various observers, according to K. C. L. Paddle (Brit. J. Child. Dis. 30: 249 (Oct.-Dec.) 1933). In his own group of 402 mentally defective children, 37 were diagnosed as congenitally syphilitic, an incidence rate of 9.2 per cent. Wassermann and Meinicke reactions were determined on the blood, and examinations of the cerebrospinal fluid included cell counts, globulin estimations, Wassermann reactions and colloidal gold tests. Of the 37 patients with congenital syphilis, 27 had positive blood Wassermann reactions, 3 had positive Meinicke reactions only; 1 had only a positive Wassermann reaction of the cerebrospinal fluid; 4 had other abnormal findings in the cerebrospinal fluid, together with physical signs and family histories suggestive of lues, and 2 children who were serologically negative were included in the series because they had clinical signs of congenital syphilis which disappeared under antisypilitic therapy. About one-third of the group of congenital syphilitics had some abnormality of the cerebrospinal fluid. No such changes were found in any one of the 29 Mongolian idiots.

Some *relationship of abnormalities of the thyroid gland to mental deficiency* was sought by J. L. Newman (J. Ment. Sc. 79: 464 (July) 1933). Histologic examinations were made of the glands of 90 mental defectives between the ages of 1 and 19 years. Considerable variations in the appearance of the thyroid were noted but there was no characteristic change which might be called typical of mental deficiency nor was there any constant difference in the glands of patients of one level of intelligence from those of another. Mongolian idiots seemed to have a diminution of active parenchyma. No relationship between the thymus and the thyroid glands could be determined, although the thymus apparently atrophied prematurely in the mentally deficient group.

*Premature birth or underweight condition at birth* were thought by A. J. Rosanoff and C. V. Inman-Kane (Am. J. Psychiat. 13: 829 (Jan.) 1934) to be definite etiologic factors leading to mental deficiency. In a comparison of 148 pairs of twins with superior intelligence and 234 pairs of twins who were mentally deficient, great differences of mental development were observed among monozygotic twins and a greater incidence of mental deficiency occurred in twins than in single births. The former finding indicated some impairment of fetal development rather than an inherited or germinal deficiency. The latter finding indicated a liability of intracranial damage at birth. Among 122 mentally deficient patients, 21 per cent. were premature or weighed less than 5½ pounds at birth. This rate was calculated to be about 8 times greater than that of the average population. Among 146 children who had been prematurely born or were underweight at birth, 10 per cent. were mentally deficient, a rate nearly 4 times greater than that occurring in groups of unselected children.

An interesting family history illustrating the difficulty in predicting the mental status of an individual patient on hereditary factors alone was reported by L. S. Penrose (Brit. M. J. 1: 10 (Jan. 6) 1934). He described the incestuous union of a feeble-minded brother and sister which was productive of normal children. The brother was definitely defective and later suffered from general paralysis. The sister, who was 8 years younger, had an intelligence quotient of 50.

to 60. The first child of this union, who died at the age of  $2\frac{1}{2}$  years, showed no signs of mental retardation. Two other children, 13 and 3 years of age, seemed to have normal mentality, and intelligence tests of the younger child substantiated this opinion

A J. Rosanoff, L M Handy, I. A Rosanoff and C. V. Inman-Kane (J. Nerv. and Ment. Dis. 80. 125 (Aug.) 1934), in an article concerning *sex factors* in intelligence, state in their conclusions that the sex distribution of intelligence is unequal, the female sex being slightly favored. Roughly, about one-fifth or one-fourth of the difference seems to be due to a sex-linked genetic factor or factors.

Many cases of both relative and absolute mental deficiency are produced by factors at work in the fetal period of life or during the process of birth. There is a great deal of evidence indicating that male fetuses are more vulnerable than female ones, both in a general way and with respect to the organ of intellectual function—the cerebrum. Therefore, there is a higher incidence of both relative and absolute mental deficiency in the male than in the female sex. The relatively greater cerebral vulnerability of the male fetus seems to account, roughly, for about three-fourths of the difference in the sex distribution of intelligence. The authors feel that there are important problems of mental hygiene in connection with pregnancy and childbirth.

**Treatment** —(O)bservations of the success of subnormal children in their communities were made by M E Shimberg and W Reichenberg (Ment Hyg 17 451 (July) 1933). The group was composed of 189 children with intelligence quotients of 75 or below, who had been observed for at least 4 years and were now 18 years of age or older. The patient's position in the community was considered as successful if he was working regularly and causing no trouble; doubtful, if he worked irregularly and caused minor disturbances but no delinquent acts leading to court action, and a failure, if he was a constant disturbance, had a court record or had to be committed to an institution. More than half of the group of 189 children had led successful lives throughout the period of observation and although 90 per cent of the group were doing unskilled types of work, 68 per cent were self supporting and 11 per cent were partially so. The mentality of the parents had no significant bearing on success or failure of their children. Children from families of higher economic levels succeeded in greater numbers than those of poorer classes. A positive relationship also existed between good personality traits and success in the community. Patients who had supervision and who followed the recommendations of the supervisor were successful in much greater numbers than those who did not. The authors concluded that individual study and care of deficient patients may make a majority of them fit for satisfactory life in a community.

A group of 18 patients with birth injuries resulting in spastic paralysis and mental deficiency were selected by E W. Martz and H N. Irvine (J Juvenile Research 18 42 (Jan) 1934) for an intensive physical and mental training. The ages of the patients varied from 8 to 50 years and their intelligence quotients from 20 to 62. The **physical training** included: (1) Teaching the patients to completely relax their muscles, (2) massage and passive motion of the extremi-

ties; (3) instruction in rhythmical active movements. **Classroom work** consisted usually of simple reading and arithmetic lessons and training in the manual arts. Ten of the patients had diplegia, 5 paraplegia, and 3 hemiplegia. In mental rating, 4 were morons, 13 imbeciles and 1 an idiot. The best physical improvement was made by the patients who were in their late teens or early twenties. Other factors which seemed to favor improvement were the degree of coöperation of the patient and length of time of treatment. Mental improvement occurred in all but 1 patient, and the 1 idiot and those belonging in the lower imbecile group made the greatest gains. There was no definite relationship between mental and physical improvement although, again, the patients in late puberty or early adult life and those exhibiting an interest in the work seemed to be favorably influenced by classroom instruction. Although none of the patients reached a stage of economic habilitation, there seemed to be a general improvement in their usefulness, cooperation, desire for sociability and eagerness to improve their condition.

Special training of this type which was given a boy 22 years old, with a mental age of 8 years and a spastic quadriplegia resulting from a birth injury, was reported by S. G. Longwell (*Ibid* 18:36 (Jan.) 1934). This patient's physical condition, ability to care for himself and general mental disposition improved under prolonged treatment. His mental age made no apparent gain.

**Prophylaxis.**—Since hereditary factors seem to play an important etiologic rôle in the incidence of mental deficiency, the most effective method of prevention of the occurrence of this condition has seemed to be **sterilization** of defective parents. In the opinion of M. T. Macklin (*loc cit*) sterilization of the mental defective will not only tend to reduce the incidence of feeble-mindedness, but unless some such measure is adopted the normal stock will be eliminated. If the assumption that heredity is the chief cause of mental deficiency is incorrect, and that environment is the important etiologic factor, the author believed sterilization would at least solve the problem of a normal child being raised in a home by defective parents.

In spite of improved facilities of institutionalization of the individuals with the lowest grade mentalities, there is very little evidence of reduction in size of families of the feeble-minded class. The conclusion reached by the Brock report (*Lancet* 1:1067 (May 19) 1934) was that reproduction by the mental defective should be discouraged and voluntary sterilization should be permitted any parent who had produced a defective child.

**MONGOLIAN IDIOCY.—Etiology.**—In a review of a group of 18 children with mongolism, which was reported by E. Stern (*Ztschr f Kinderh* 55:372 (Sept) 1933), the *ages of the parents* at the time of the birth of the children was under 30 years in only 3 instances; the mother was over 35 years in 7 instances, the father was over 35 years in 13 instances, one of the parents was over 40 years of age in 5 instances. Six of this group of mongolian idiots were first-born children, 1 was the twelfth child and 1 the seventh while 2 were the sixth children. In 6 cases the mother had had one or more miscarriages previous to the birth of the patient. Labor had been normal for 10 mothers of the group; was prolonged in 5 cases, was aided by forceps in 2. In one instance



a Cesarean delivery was necessary. Asphyxia at birth had occurred in 3 babies, but usually the size of the child had been normal or below. *Unusual hereditary factors* could not be demonstrated in the family histories of 13 children of the group. In one of the remaining number of children the father had been alcoholic, and in another the father had used opium. Hereditary factors were thought to play a very little rôle in the etiology of mongolism.

In one-half of a group of 8 infants with mongolism, a history of exhaustion or youthfulness of the parents was found by A. Santillana (Arch. de méd. d. enf. 36:615 (Oct.) 1933) and he believed mongolism resulted from a defective germ plasm. The parents of one of his patients were very young, were cousins in another instance, were syphilitic in a third, and had had 5 or 6 children previously in 3 other instances.

*Mongolism in twins* is a rare occurrence and of interest from an etiologic standpoint. According to S. E. Torsten Lund (Am. J. Dis. Child. 46:811 (Oct.) 1933), there have been only 6 previous reports of mongolism occurring in both individuals of monzygotic twins. There have been 38 reports of dizygotic twins in which mongolism has occurred in one of each pair. The twins reported by the author were the eleventh and twelfth children of the family and at the time of their birth the father was 51 years old and the mother 44. The delivery was about 3 weeks premature and the use of forceps was necessary. At the age of 10 years these twin girls had considerable mental retardation and many of the physical characteristics of mongolism. Proof that they were identical twins was established by the similarity of the color of their eyes, hair and general features, and the configurations of their finger prints.

An instance of mongolism of only one twin of a pair was observed by G. Mouriquand and J. Schoen (Arch. de méd. d. enf. 36:620 (Oct.) 1933). There was a difference in sex of the two twins and not until they were several months old did the parents notice that the girl was not gaining in weight or developing as rapidly as the boy. According to the authors, 21 instances of twins of different sexes have been reported in which one of each pair had mongolism and the other was normal. In addition, there are reports of 24 instances of twins of the same sex in which one had mongolism and the other was normal.

**Diagnosis**—To the numerous clinical signs of mongolism, A. Bleyer (Am. J. Dis. Child. 47:342 (Feb.) 1934) has added 3 more and it is his opinion that many more abnormalities might be detected by careful study of these patients. He calls attention to the marked degree of elasticity of the skin, most readily noticed on the back of the neck, where folds of the skin may be lifted away from the underlying structures. The labia majora of mongoloid females was noticed to be unusually full and rounded, and on the chest, the nipples often appeared as round beads on the skin, with an absence of the characteristic areola. These last 2 conditions were not thought to be pathognomonic of the disease, but merely accompanying phenomena.

**Treatment**.—Sixteen children with mongolism were treated by E. Stern (*loc. cit.*) with **x-ray irradiation**, **thyroid** and **pituitary extracts** and **lipatren** which is a lipid material containing iodine. This therapy had no effect on 7 of the group, gave questionable results in 2, and seemed to cause improvement

in the remaining 7. The children of this last group seemed to become more active, to take greater interest in their surroundings, and they spoke more distinctly with vocabularies of increased size.

The 8 infants with mongolism treated by A. Santillana (*loc. cit.*) with irradiated ergosterol and thyroid extract showed no apparent improvement of their mental condition, but their general health seemed better; the fontanelles closed earlier; dentition was accelerated; and their appetites were improved.

**X-ray therapy** was employed by J. Jochims (Arch. f. Kinderh. 100:27 (July 18) 1933), in the treatment of a group of 23 feeble-minded children, of whom 11 were mongolian idiots ranging in age from 4 months to 11 years, 8 were endogenous imbeciles, 1 a microcephalic, 2 were postencephalitic defectives and 1 was mentally retarded as a result of a cerebral form of poliomyelitis. The irradiation was given according to the technic of von Wieser with 5 exposures of the skull at weekly intervals over a period of 5 weeks. After a rest period of 4 weeks the treatment was repeated. The rest periods were gradually prolonged and the total course of treatment for a single patient extended over a period of 9 months to 2 years. The results seemed to be limited to the changes of behavior of the patients. Those who were restless and hyperactive were frequently made more quiet, those who were dull and apathetic were stimulated. The author believed that any other improvement of the children's condition could be attributed to this change in temperament. The effects of the therapy were not always permanent but there never were any harmful results observed.

**MEASLES.**—Infants under 6 months of age rarely contract measles and this early immunity has been explained by the presence of protective antibodies which have been transmitted to the baby from its mother. Recent exceptions to this general rule have been reported by J. L. Kohn (J. Pediat 3 176 (July) 1933), who had observed several instances of *measles in newborn infants*. Two mothers who were in the incubation stage of the infection when their infants were born, developed the rash a few days later. The children contracted the disease on the ninth and tenth days, respectively, after the onset of their mothers' illness. Two other mothers contracted the disease shortly after parturition and the infants developed the first symptoms of the disease 10 and 11 days later. The course of measles in these 4 infants did not differ materially from that of older infants and children. On the other hand, 2 infants who were born of mothers who had clinical signs of measles at the time, were separated immediately from their mothers and, although untreated, did not develop measles at any time while under observation. Similar instances have been reported in the literature. One child born of a mother in the last 6 days of the incubation period of measles was given 10 c.c. of human convalescent serum when 17 days of age and was protected from the disease.

**Second Attacks.**—Considerable controversy has arisen lately in regard to the possibility and frequency of second attacks of measles. H. Zischinsky (Jahrb. f. Kinderh. 142.43 (Feb.) 1934) claimed that among the 11,000 measles patients who had been under his care there was not a single instance in which he felt that a definite second attack of measles had occurred. Certain

difficulties of differential diagnosis between measles and rubella were thought to have confused some clinicians and the unusual forms of measles caused by the injection of convalescent serum have recently made diagnosis more difficult.

Other clinicians who have not observed second attacks of the disease in the same patient were K Ochsenius (*Kinderarztl. Praxis* 5:5 (Jan) 1934), P. Selter (*Ibid.* 5:14 (Jan) 1934), K Kleinschmidt (*Ibid.* 5:12 (Jan. 1934), W Birk (*Ibid.* 5:64 (Feb) 1934), and Mettenheim (*Ibid.* 5:64 (Feb.) 1934).

An unusual number of patients with second attacks of measles was reported by S Wolff (*Ibid.* 4:456 (Oct) 1933). He had observed 12 to 15 patients who had had 2 attacks which occurred within a few months of each other. In one child 3 definite measles infections had occurred at intervals of 1 year, at ages of 4, 5 and 6 years. Each of the patients reported had characteristic Koplik's spots, conjunctivitis, an enanthem, a typical exanthem, a bronchitis, and the usual fever curve, all of which were personally observed by the author.

Other clinicians have noted rare examples of a repetition of measles in the same patient. Rudder (*Ibid.* 5:62 (Feb) 1934) mentioned 2 such instances in which a year or more had elapsed between attacks. G Jurgens (*Ibid.* 5:65 (Feb) 1934) had seen one such patient. E Glanzmann (*Ibid.* 5:108 (Mar.) 1934) differentiated between a relapse within a short time after the primary illness and a second attack occurring after a much longer period of time. He had observed both types of recurrence. Von Groer (*Ibid.* 5:110 (Mar) 1934) reported 2 instances of second attacks of measles which he had seen during 20 years of observation. In one patient a period of 3 years elapsed between the 2 illnesses and in the second patient the period of time was 4 or 5 years.

*Relapses* of measles, occurring within a month after the original infection, were observed in 2 instances by Apert and Y Kermorgant (*Bull. et mém. Soc. méd. d'hop. de Paris* 49:782 (June 19) 1933). One patient had the typical measles exanthem twice within a period of 12 days and the other at an interval of 4 weeks. *Recurrences* of measles after periods of time greater than a month occurred in 3 instances. One recurrence developed in a patient 6 months after the first attack, in the second patient 4 months later, and in the third patient 10 years after the first attack.

A summary of many of the opinions expressed in regard to the recurrence of measles was made by H Opitz (*Kinderarztl. Praxis* 5:213 (May) 1934). From the divergence of opinion expressed and from his own experience he was inclined to believe that second attacks of measles occurred in rare instances. Mistaken diagnoses must be borne in mind as a source of error and he called special attention to the added difficulty in making a diagnosis of very mild attacks of measles when the course of the disease has been modified by serum therapy given early in the incubation period. Such modified attacks of measles may not produce sufficient active immunity in a patient and thereby render him susceptible to a second attack.

**Diagnosis.**—In the observation of early symptoms and signs of measles, E Mayerhofer (*Ztschr. f. Kinderh.* 56:42 (Feb) 1934) noted that during the incubation period of the disease there were elevations of temperature in the first

to fourth day which resembled the "nonallergic" state. Later, after the fourth day, a rise in fever sometimes occurred which was thought to be allergic in nature. The *angina* of measles which occurred during the fourth to the eighth day, but more frequently during the ninth to the twelfth day, before the appearance of Koplik's spots, coincided in time with the occurrence of abdominal pain of pseudoappendicitis. During these stages, large numbers of giant cells have been seen both in the tonsils and in the appendix. These cells, which were thought to have originated from the endothelial lining of the blood-vessels, cause a congestion within the vessels and an exudation of hemoglobin. When this happens in the throat, it leads to the chocolate appearance described by other clinicians. This angina may be an allergic reaction involving all of the mucous membranes of the mouth. Although similar anginas have been noted in other illnesses, a knowledge of this sign together with the course of the temperature and the occurrence of abdominal pain may be valuable in detecting early measles infections in institutions where exposures are known.

An early diagnostic sign of measles, previously described, has been emphasized lately by R. Meyer (Rev. franç. de pédiat. 10:85, 1934). It consists of a *redness and congestion of the semilunar fold of the eye* which often precedes the generalized conjunctivitis and the Koplik's spots. The caruncle of the eye was not usually as much involved as the semilunar fold at this stage of measles. As the Koplik's spots appeared, the redness of the semilunar fold usually diminished and sometimes little white spots similar to Koplik's developed later. The occurrence of this sign and the time it appeared seemed to differ in different epidemics and in different children. The author has also noted, during the first hours of fever of an attack of measles, a *roughness* resembling a thin membrane *on the tonsils*. On the bluish red surface were very small white points like Koplik's spots. About 12 to 24 hours later, the spots disappeared and the tonsils became more red and congested.

An extensive study of the blood picture in measles has been made by H. Bjorn-Hansen (Acta paediat. (Supp. I) 14:1, 1932). *Changes in the function of the bone-marrow, the lymphatic system and the reticulocytic systems* were detected by the presence of various types of neutrophils, lymphocytes and monocytes in the circulating blood. During the incubation period, up to a week before the beginning of the rash, there was an increase in the total number of leukocytes to 10,000 to 14,000 and, thereafter, there was a decrease in the numbers of both lymphocytes and granular leukocytes. An absolute decrease in the number of neutrophils and a shift to the left occurred in the week preceding the rash and reached the minimum at the height of the exanthem. As many as 80 per cent of the neutrophils had band-shaped nuclei or were young forms. This was more intense than in tuberculosis and the shift continued longer when complications occurred. The lymphocytes diminished in number during the height of the infection and young forms (Turk cells) were observed, but this decrease was of shorter duration than the neutropenia. Recovery occurred with fading of the rash. The monocytes throughout did not change in their relationship to the other cells.

The author explained these phenomena by an increased stimulation of the bone-marrow and lymphatic system at first, but this function became exhausted during the exanthem and the complications of measles. During convalescence the function of the hematopoietic system was slowly restored.

The injection of milk during measles was followed by less response than usual from the hematopoietic system which was a reaction similar to that observed in patients suffering with sepsis. In spite of the enlargement of the lymph nodes and spleen, the lymphocytes apparently could not be produced fast enough to take care of the infection. The diazoreaction also demonstrated a destruction of cells of the blood or nuclear tissue elsewhere in the body, but it was impossible to determine whether destruction of the lymphocytes occurred in the peripheral circulation or in the spleen.

The absence of bone-marrow function may also account for the poor development of immune bodies as manifested by numerous complications that measles patients develop. There seemed to be a resemblance between the blood picture of measles and serum sickness and it was thought possible that the toxin of the disease does not alone account for the destruction of cells, but that an anaphylactic process determines the destruction.

**Complications.**—A review of 13 cases of *encephalitis* following measles was made recently by M. G. Peterman and M. J. Fox (Am J Dis Child 46 512 (Sept) 1933). These patients were observed over a period of 5 years, from 1927 to 1932. Nine of them fell sick during a 3-month period in 1932. The ages of the children of the entire group ranged from 10 months to 8 years and death occurred in 43 per cent. The typical symptoms of *encephalitis* began 2 to 6 days after the onset of the measles rash in all but one child who did not have symptoms until 8 days after the rash. The most common symptoms were stupor and drowsiness (12 patients), convulsions (3 patients), neck rigidity (5 patients), and a positive Brudzinski neck sign (3 patients). A leukocytosis of 12,000 to 16,000 cells was accompanied by a polymorphonuclear increase of 74 to 84 per cent. The cerebrospinal fluids were clear, under increased pressure, in 7 instances, contained 40 to 98 per cent. of lymphocytes, and gave a positive globulin test in 6 cases. Autopsies of 3 patients showed congestion of the blood-vessels of the pia mater on gross examination, and microscopically, a fibrotic thickening of the vessel walls, hyperplasia of the endothelium with small thrombi and petechial hemorrhages in scattered areas. The neuroglia was thickened about the involved vessels and nerves and some of the pyramidal cells were shrunken, degenerative or had disappeared entirely.

The most effective method of treatment in 1 instance seemed to be **spinal drainage** and intravenous injections of 5 c.c. ( $1\frac{1}{4}$  drams) of a 20 per cent. **magnesium sulphate solution**, intramuscular injection of 10 c.c. ( $2\frac{1}{2}$  drams) of a 50 per cent. solution and the oral or rectal administration of 2 ounces (60 Gm.) of the same drug. **Sedatives** and **chloroform anesthesia** were required to control the convulsions in this 1 instance.

According to the statistics reported by C. C. Elliott and A. Elliott (Brit M J. 2:734 (Oct 21) 1933), the incidence rate of *encephalitis* in Berlin was 0.4 per cent. among 5940 patients with measles. The mortality rates were about 10

per cent., but an additional 65 per cent. of encephalitis patients had some residual injury of the central nervous system. They reported an instance of the disease which occurred in a boy 18 years of age who developed symptoms of restlessness, unconsciousness, fever, and abnormal reflexes on the third day of an attack of measles. The cerebrospinal fluid contained 74 cells per c.c., most of them lymphocytes, the globulin was increased in amount but no microorganisms were found. Two months later, recovery was practically complete.

Another instance of *encephalitis* following measles was reported by G. Blechmann and J. Toupet (Bull. Soc. de pédiat. de Paris 32:68 (Jan.) 1934). A boy, 10 years of age, developed headache and irritability on the fourth day after the onset of the measles and within a short time had signs of meningeal irritation, fever, unconsciousness and certain abnormal reflexes. Within 3 weeks, great improvement was noticed and at the end of 4 months recovery was complete. An instance of encephalitis, which developed 8 days after the onset of measles in a child 3 years of age was reported by A. M. McCausland and S. J. McClendon (Arch Pediat 51:178 (Mar) 1934). The symptoms of convulsions, vomiting, inability to swallow and coma marked the onset. The cerebrospinal fluid contained no increase in the number of cells but in the eye grounds there was evidence of a papilledema and later a temporary paralysis of the legs developed. An encephalogram was useful in this patient in eliminating the possibility of hydrocephalus and brain tumor. The child made an uneventful recovery.

*Edema of the larynx* during measles was observed in 3 children, 3 to 7 years of age, by K. S. Oliver and E. L. Turner (J. A. M. A. 101:1801 (Dec 2) 1933). The difficulty of breathing and cyanosis began 6 to 7 days after the onset of the rash in 2 instances and a few days later in the third. **Tracheotomy** gave relief to 2 children and they made a complete recovery. The third child died 8 hours after the operation.

Further x-ray studies of the chests of children with measles were reported recently by J. L. Kohn and H. Koiransky (Am. J. Dis. Child 46:40 (July) 1933). In addition to anterior-posterior views, x-rays of the right and left lateral positions were taken of 59 children with measles. The ages of these children were 1 to 10 years and all were thought to be free from tuberculosis. *Lymph nodes* anterior to and below the bifurcation of the trachea were usually *enlarged* during the height of the attack of measles. Occasionally the glands posterior to the trachea were also enlarged. *Interlobar pleurisy* with thickening was observed in 11 instances, but subsided considerably during the patient's convalescence. Pleural involvement was usually associated with evidence of pulmonary infiltration, but it was difficult to determine whether or not the former was a result of the alveolar involvement. In children under one year of age, the x-ray findings were similar to those reported previously in that 62.5 per cent. of the group had shadows suggesting pulmonary infiltration.

In 17 children who had received human convalescent serum 2 to 18 days before the fever of measles began, 13 had no x-ray evidence of infiltration of the lungs. The remaining 4 patients had received the serum late in the incubation period and they contracted severe infections with demonstrable *pulmonary lesions*. Even though pulmonary infiltration could not be detected in the protected group,

hilar gland enlargement and pleural thickening were noted. Postmortem examinations of the lungs of children dying of measles showed marked peribronchial infiltration with small lymphocytes and large mononuclear cells. The regional nodes were hyperplastic and a similar mononuclear reaction occurred.

**Treatment.**—**Citrated whole blood** was used by R. M. Lord (J. Pediat. 3:509 (Sept.) 1933) for the protection of children 3 months to 6 years of age who had been exposed to measles. The blood was taken from adult donors, usually brothers or sisters of the patient, in quantities of 5 to 25 c.c., to which 3 c.c. of 2 per cent. sodium citrate were added. The injections were usually given on the eighth day after the patient's exposure to the disease, in order to allow an attenuated form of measles to develop. In one group of 29 patients mild attacks of the disease developed in the most of the treated children and none had complications. In another group of 38 patients, 8 escaped infection, 24 developed mild attacks and 6 severe ones. A third group of 17 patients of an orphanage received this treatment and 10 developed mild attacks, while 7 escaped the disease. In a fourth group of 5 patients the course of the disease was apparently modified greatly by the human serum injections.

Widespread use has been made of the **blood serum of immune individuals** in the *prophylaxis* of measles in Russia. S. J. Shafershteyn (Kinderarztl Praxis 4:461 (Oct.) 1933) stated that measles in the U. S. S. R. has been very severe recently. The epidemics have been extensive and the mortality rate of this disease was greater than that of scarlet fever and diphtheria together. Because of the large number of children gathered together in various institutions, crèches, etc., prophylactic treatment against measles was very necessary. Blood was usually taken from the parents, but occasionally it was obtained from professional donors and from placentas. It was expected that the prophylactic doses would be prepared and distributed from central stations.

From **normal human placentas, extracts** have been made which contain some of the antibodies usually found in the blood serum of immune adults. It has been stated by C. F. McKhann and H. Coady (South M. J. 27:20 (Jan.) 1934) that further refinements of these extracts have removed the foreign inert material, leaving the pseudoglobulins which contain most of the antibodies. Extracts from various placentas were pooled and the total nitrogen content was determined so that a fairly accurate index of the potency could be ascertained. In the treatment of measles or in the prevention or attenuation of an attack, the placental extracts were administered in much the same manner as injections of convalescent serum or immune adult blood. Of a group of 100 susceptible children who were exposed to the disease, injections of the extract early in the period of incubation apparently protected 91. Of the remaining number, 4 developed the disease in mild forms.

Since the observations of McKhann and others that the immune bodies in placental extracts were globulins, S. Karelitz (Proc Soc Exper Biol and Med. 31:793 (Apr.) 1934) has extracted the globulin fraction from blood serum of immune adults. Injections of this **globulin fraction** were frequently very painful but protected exposed susceptible children as well as the whole blood injections.

**Pyramidon** has been a favorite drug of many clinicians for the treatment of measles. Considerable variation of opinion has arisen in regard to its effectiveness. G. Blechmann (Bull. Soc. de pédiat. de Paris 31:368 (July) 1933) found that it hastened the disappearance of the rash in some instances but in many other patients it had no effect on the outcome of the illness and did not check the occurrence of complications.

**Human convalescent serum** was employed in the treatment of *encephalitis* following measles in a child, 7 years of age, by B. P. Storts (Southwestern Med 17:330 (Oct.) 1933). The serum was given intraspinally on 2 occasions in doses of 8 c.c. and 6 c.c., on the second and third days of the encephalitic symptoms. Other treatment consisted of **sedatives** and **dextrose** and **insulin** injections. The child made a rapid recovery.

**MUMPS.**—During the past year there have not been many contributions to the literature on mumps. Y. Kermorgant (Progrès méd., p. 1102 (June 17) 1933) believes he has demonstrated that he is able to keep and cultivate the virus of mumps. He cites animal experiments in support of this contention.

**Complications.**—Many of the contributions, as usual, are concerned with reports of complications, particularly neurological. C. B. McKaig and H. W. Woltman (Arch Neurol and Psychiat 31:794 (Apr.) 1934) report an instance of *myelitis* without meningitis following mumps in a girl, aged 16 years. There was marked loss of ability to use the hands and complete flaccid paralysis of the trunk and legs. She also had relaxation of the anal sphincter and atony of the bladder musculature. There was no improvement 18 months after the onset.

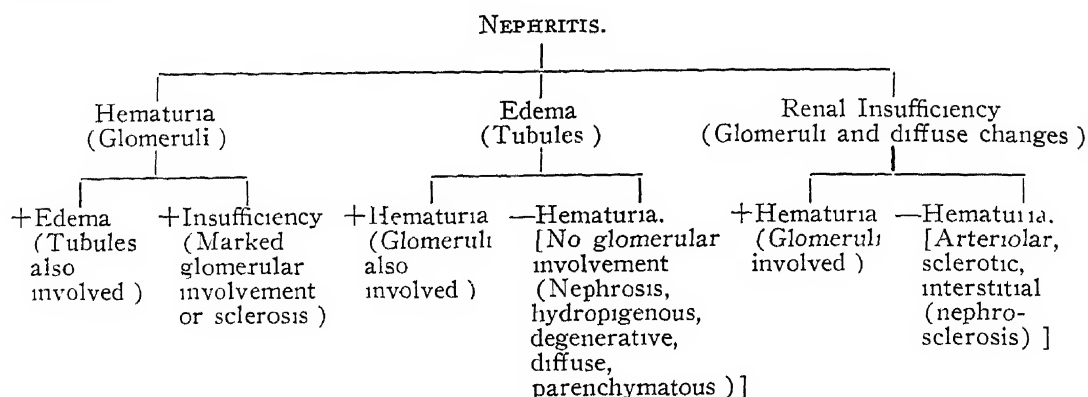
A case of *meningomyelitis* was also reported by C. Kousmine (Schweiz. med Wchnschr 64:235 (Mar. 10) 1934). In reporting a case of post-mumps *encephalitis* without meningitis, A. Lénierre, J. A. Lièvre and Pham-Huu-Chi (Bull. et mém. Soc. méd. d'hôp. de Paris 50:109 (Feb. 5) 1934) argue that this may be taken as additional evidence that the virus of mumps has a direct affinity for the parenchyma, contrary to the common conception of localization in the meninges and extension to the parenchyma.

**NEPHRITIS IN CHILDREN.—Classification.**—The number of different classifications of nephritis bears testimony to the difficulties in such an undertaking. An etiologic classification is obviously an impossibility. Most classifications are based on pathologic changes or a combination of these with etiologic data and symptoms. Clinically, it is not always possible to predict the existing pathology. For this reason and since there are more or less distinct, clinically recognizable kidney diseases which are quite different in respect to therapy and prognosis, there would seem to be logic in a clinical approach which recognized pathologic and etiologic factors as far as possible.

A. Graeme Mitchell (J. Med 14:401 (Oct.) 1933) has no particular fault to find with the various existing classifications of nephritis, nor does he offer a new one. In fact, he states that he can fit his knowledge of the nephritides into any of them. However, he does emphasize the importance of thinking in clinical terms. To him 3 symptoms stand out: hematuria, edema, and all those phe-



nomena which could be included under the term renal insufficiency. He offers a schematic outline based on these 3 symptoms which is as follows :



**Treatment.**—Good results with an **exclusive sugar diet** in acute nephritis in children is reported by Z. von Bókay and L. von Kostyál (Archiv f Kinderh 100: 123 (Sept 29) 1933). The children are given only 250 to 400 Gm ( $8\frac{1}{3}$  to  $13\frac{1}{3}$  ounces) of malt sugar or potato sugar for a number of days, usually until improvement sets in. After that, some fruit and a little water are added, and gradually a mixed diet is introduced. The authors report that patients with acute nephritis recover within 15 days and those with chronic nephritis or nephrosis within 15 to 30 days. The exclusive sugar diet seems to rest the kidney and thus promote recovery. It is also supposed that it exerts a favorable influence upon disturbed water balance.

P. Gautier (Rev franç de pédiat 9 605, 1933) has observed remission of the symptoms of nephrosis in 2 children during acute infections. One child who had measles had a return of the nephrotic symptoms some time later, the other child had no evidence of nephrosis 5 months after an attack of acute mastoiditis. Gautier believes that the improvement was due to the fever and suggests the possibility of using **fever-therapy** in cases of nephrosis.

**RENAL RICKETS.**—The frequent occurrence of dilatations of the urinary tract in children with renal rickets or dwarfism is emphasized by the report of A. Ellis and H. Evans (Quart J Med 2 231 (Apr) 1933). Observations of the urinary tract were made in 17 of 20 cases of renal dwarfism. In 14 there were varying degrees of dilatation. The urinary retention seemed to be at the level of the urethrovesical sphincter. No cause of obstruction or lesion of the nervous system was found. It was suggested that there might be a disorder of the neuromuscular mechanism controlling the urethrovesical sphincter.

An instance of renal rickets associated with parathyroid hyperplasia has been reported by F. S. Langmead and J. W. Orr (Arch Dis Childhood 8 265 (Aug) 1933). The bony changes were characterized by marked osteoporosis of the type described as honeycomb, stippled, or woolly. The authors feel that there is more than a chance significance between the parathyroid hyperplasia and this type of bony change. They suggest that the osteoporosis is due to osteoclastic resorption which is the result of secondary parathyroid activity. Unfortunately, they do not have the confirmatory support of a blood calcium determination.

**NEWBORN, DISORDERS OF.—ATELECTASIS.**—An interesting study of atelectasis in the newborn has been conducted by S. Farber and J. L. Wilson (*Am. J. Dis. Child* 46: 572 (Sept.) 1933). As the result of their observations, they state that, contrary to common opinion, expansion of the lung is not complete after the first breath of the newly born infant and, further, that a certain degree of initial atelectasis is probably physiologic for several days after birth. Since a variable amount of atelectasis is normally found within the first few days of life, the authors do not believe that the cause of death should be ascribed to this factor unless it is extensive. In such an instance the cause of the atelectasis should be demonstrated.

A method for the differentiation of atelectasis in lung tissue that has never expanded from atelectasis in previously expanded lung tissue but subsequently collapsed, so-called "resorption atelectasis," is described. Histologically, it is shown that the flattened lining epithelial cells lining the alveoli do not return to the cuboidal shape of their nonexpanded stage even though resorption atelectasis occurs. The importance of recognizing this type of atelectasis is in the implication that expansion has once taken place, and that subsequently there has been some interference with respiration.

While any type of atelectasis may be found in premature infants, solid, incompletely developed areas of lung tissue may be present which superficially may resemble atelectasis. Such areas represent immaturity and not true atelectasis.

These same authors in a separate article (*Ibid.* 46: 590 (Sept.) 1933) consider the factors affecting the pathogenesis of atelectasis in the newborn. In the first place, they have shown that cohesion of the moist surfaces of the air passages in collapsed and airless lungs offers a considerable obstacle to the entrance of air, and that a relatively great force is required to overcome this cohesion and to separate the bronchial and alveolar walls during the initial expansion of an atelectatic lung.

They group the factors which may be operative in interfering with the normal mechanism of overcoming this cohesive tendency of the moist lung surfaces under 3 heads:

"1. An imperfectly developed or an injured respiratory center which, not responding to normal respiratory stimuli, fails to bring about repeated and sufficiently vigorous respiratory efforts. Evidences of immaturity of the central control of respiration in the brain stem may be detected in many premature infants. Damage to the medulla due to trauma, hemorrhage or direct asphyxia is a well-known and frequent condition in the newborn.

"2. An imperfectly developed thoracic mechanism such that the contraction of the intercostal muscles and the bony resistance of the thorax do not furnish an effective *vis a tergo* for the efficient action of the diaphragm. This is especially seen in premature infants.

"3. Bronchial obstruction due to aspiration of the contents of the amniotic sac, mucus or blood. This we have shown may be of great importance in full-term infants, less frequently so in premature infants; only rarely is it, in itself, however, a complete cause of extensive and persistent atelectasis."

**BLOOD-PRESSURE.**—The blood-pressure of 100 newborns has been taken on each of the first 4 days of life by J E Bowman (*Am J Dis Child* 46:949 (Nov.) 1933). The averages for this group were as follows.

Days.	BLOOD-PRESSURE mm of mercury.	
	Sys	Dias
1 .. . . .	55	/ 38
2 . . . . .	60	/ 41
3 ... ..	60	/ 42
4 . . . . .	60	/ 44

The determinations were made with the Pachon oscillometer, with a 5 x 20 cm cuff placed about the right leg. In general, the systolic blood-pressure was higher in babies of greater birth weight, while there was little variation in the diastolic.

*Fluid in Trachea*—The effect of posture upon the movement of intratracheal fluid in paralyzed cats (kept alive in a Drinker respirator) has been studied by D P Murphy (*Am J Obst and Gynec* 27:118 (Jan.) 1934). On the basis of these experimental observations he concludes that, as a prophylactic measure against the inhalation of fluid which is presented in the trachea of the newborn, the position of the body be maintained at an angle of at least 15° with the horizontal, with the head down.

**MENINGITIS.**—An instance of meningitis in the newborn due to a member of the paracolon group of organisms is reported by C. M. Pounders (*J Pediat* 4:752 (June) 1934). Meningitis in the newborn is not particularly frequent, although the author suggests that, because of the indefinite symptoms, it may be more frequent than commonly supposed, and may be one of the unexplained causes of death. When the invading organism is one of those commonly found in the intestinal flora, the author suggests a possible explanation of the pathogenesis. The argument which follows is taken in part from an article by J V Cooke and H H Bell (*Am J Dis Child* 24:387 (Nov.) 1922). The organisms gain access to the digestive tract during or shortly after birth. A highly permeable intestine permits them to pass rather easily into the circulation, and the lack of developed general immunity offers an insufficient obstacle to their circulation in the blood stream. Intracranial injuries probably result in points of low resistance where the organisms may lodge and cause meningitis.

**PHRENIC NERVE PARALYSIS.**—Two instances of phrenic nerve paralysis in the newborn, associated with Duchenne-Erb's paralysis, are reported by J L Stein (*J Pediat*. 3:471 (Sept.) 1933). Seven similar cases, found in the literature, are reviewed in this article. The author suggests that phrenic nerve paralysis in the newborn may be more frequent than has been supposed. He recommends looking for it in all cases of Erb's paralysis, since in one of his cases there was a complete absence of symptoms referable to the respiratory system. The appearance of cyanosis and dyspnea in a newborn infant shortly after a difficult birth should be sufficient reason to suspect injury of the phrenic nerve. If such is the case, the usual findings are similar to those observed in massive pneumonia or pleurisy, but with normal temperature and a good general

condition. Fluoroscopy will reveal a high position of the diaphragm on the affected side and a typical paradoxical movement of the diaphragm (Kienbock phenomenon) in breathing, the affected side ascends during inspiration while the normal side descends, this being reversed during expiration, like the sea-saw of a pair of scales in perfect synchronism. The respiration may be irregular and rapid and often there may be periods of severe air hunger. The type of breathing, unlike that of newly born infants, is thoracic. The heart is displaced toward the affected side and downward.

Five additional cases of phrenic nerve paralysis are reported by R. M. Tyson and J. E. Bowman (*Am. J. Dis. Child.* 46: 30 (July) 1933). One of their cases did not have an associated brachial paralysis. They also review the literature and mention 3 case reports not included by Stein. Two of these cases also had an Erb's paralysis.

**PREMATURITY.**—The effect of environment on the growth and development of premature infants has been observed in the Boston Infant's Hospital by K. D. Blackfan and C. P. Yaglou (*Am. J. Dis. Child.* 46: 1175 (Nov) 1933). In recent years the infants have been kept in a unit in which the temperature, humidity and ventilation were kept under automatic control by a central air-conditioning system. Comparative analyses were made from the observations on infants kept in this air-conditioned unit with those on infants treated over a 3-year period in the older unconditioned nursery.

From the data thus secured they drew certain conclusions, which in part, are as follows:

1. The humidity best suited to stabilizing the body temperature of premature infants appears to be about 65 per cent, with a temperature ranging from 75° to 100° F (23.8° to 37.8° C), depending in some degree on the general constitutional state of the infant and the body weight. A humidity of 30 per cent was not compatible with stability of body temperature and often resulted in certain untoward effects.

2. The body temperature of the premature infant was controlled more regularly in the air-conditioned unit than in the unconditioned rooms.

3. Body temperature and fluctuations in body temperature under controlled air conditions were found to be related to body weight. Lower temperatures (about 98° F to 36.7° C) with a greater fluctuation were the rule in the low weight group. Attempts to raise the temperature of small infants to the supposedly normal level of 98.6° F (37° C) are not only not necessary, but may be detrimental to proper growth and may even result in death.

4. Infants kept in the air-conditioned unit under relatively high humidity had a lower initial weight loss, the period over which this weight loss occurred was less, and the infants more rapidly regained their birth weight than did the occupants of the unconditioned nursery. In these respects infants kept under low humidity were in intermediary positions.

5. The maximum gain in weight in infants weighing less than 5 pounds occurred under high humidity in the conditioned nurseries. The gain in weight was less under low humidity and in the unconditioned nursery.

6. Whereas, infants weighing less than  $4\frac{1}{2}$  pounds gained more rapidly in high than in low humidity, the reverse was true of infants who weighed  $4\frac{1}{2}$  pounds or over.

7. The maximum rate of growth in length occurred during the first and second months. The growth in length was affected by environmental changes in the same way as was the gain in weight.

8. Similarly, abnormal symptoms referable to the digestive tract occurred more often in infants of low weight who were kept in the unconditioned nursery or in the conditioned nursery under low humidity.

9. The mortality rate varied according to weight, age, sex and the general constitutional state of the patients. The gross death rate varied inversely in relation to the weight and age on admission. In all instances the mortality was lower in the conditioned nurseries than in the unconditioned nursery and lower under high than under low humidity. The most significant lowering of the gross mortality was in infants of the lowest weight groups.

10. Acute and chronic infections accounted for 70.3 per cent of the total number of deaths in the unconditioned nursery and for 31.9 per cent of the deaths in the conditioned nurseries. The general net mortality rate from infection was, respectively, 26.5 per cent for those infants who were kept in the unconditioned nursery, 9.7 per cent in the conditioned nursery with low humidity, and 0 per cent in the conditioned nursery with high humidity.

While the authors recognize that improved methods of handling premature infants will account in part for the decreased mortality of the more recently treated infants in the conditioned units, they do believe that the decrease is in part attributable to the environmental factors. The differences in growth and mortality between those infants kept under high and low humidity is strong evidence in favor of the environmental influence. They believe that body weight is the most important single criterion for determining the environmental requirements of premature infants.

According to A. Rocha (Brasil-Medico 47:583 (Aug. 19) 1933, J. A. M. A. 101:1520 (Nov. 4) 1933), the concentration of follicular hormone increases during pregnancy, to reach its maximal amount in the last days of the full-term period. After delivery, the hormone diminishes in quantity and disappears within a week. From this it is deduced that folliculin is important in the development of the fetus during the last days of intrauterine life and should be artificially administered to infants born prematurely. Instances are quoted of gains in weight in the first 11 days of life of premature infants treated with folliculin, as contrasted to a loss of weight in the same period of those not so treated. In general, the dose to be injected is 100 units of folliculin per kg ( $2\frac{1}{2}$  lbs) of body weight.

#### RESUSCITATION IN.—*Intracardiac Injection of Epinephrine.*—

The revival of 2 apparently stillborn infants by intracardiac injections of epinephrine is reported by S. A. Cameron (Mil. Surgeon 74:140 (Mar.) 1934). The use of epinephrine is recommended when signs of circulatory failure appear during protracted second stages of labor. If no fetal heart sounds are heard and no fetal movement noted for some time prior to delivery, it is useless to attempt

resuscitation by this means. He cautions that when signs of danger to the infant are evident, delivery must be accomplished as rapidly as possible, and if the infant is asphyxiated, or its cord pulseless, then the intracardiac injection is indicated. The dose used by the author was 0.3 c.c. (5 minims) of 1:1000 solution of epinephrine.

**RUPTURE OF STOMACH.**—*Diagnosis.*—To the 9, previously reported, cases of rupture of the stomach in newborns, E. C. Dunham and R. M. Goldstein (J. Pediat. 4: 44 (Jan.) 1934) have added 2 more cases. Recognizing the difficulties in diagnosing the rupture or the lesions leading to it, they recommend that x-ray examination of the abdomen should always be made before the administration of barium. By this means the presence of free air in the peritoneal cavity—evidence that rupture has already taken place—may be determined.

**TETANY.**—Tetany in the newborn occurs infrequently. In fact, a good many observers doubt its existence in the first 2 or 3 months of life. In view of this opinion, the report of 5 cases of tetany occurring within the first 9 weeks of life, one at 18 days, by H. L. Maslow (Arch. Pediat. 50: 768 (Nov.) 1933) is of interest. A. G. Mitchell and F. E. Stevenson (J. A. M. A. 99: 1502 (Oct. 29) 1932) have called attention to the fact that Chvostek's facial sign may be present in apparently normal newly-born infants whose blood calcium and electrical reactions are within normal limits. In Maslow's 5 cases the blood calcium was, in each instance, lower than 7.5 mg per 100 c.c. of blood. Four of the cases had an increase of the inorganic serum phosphorus. One infant was particularly resistant to intensive treatment with calcium and vitamin D milk, but **parathormone** was very effective in raising the serum calcium.

That certain of the symptoms attributed to cerebral birth injury may also be the result of tetany in the newborn is the contention of W. R. Shannon (Am. J. Obst. and Gynec. 27: 830 (June) 1934; Arch. Pediat. 51: 23 (Jan.) 1934). Stating that peripheral edema and cerebral edema are part of the tetany syndrome in the newborn, he says that such symptoms of cerebral birth injury as lethargy, cyanotic attacks, irregular breathing, slow pulse, bulging fontanelles, muscular twitching, projectile vomiting and convulsions may be due to tetany and that the diagnosis of birth injury is often incorrectly made. He believes that tetany in the newborn is the result of insufficient ionized calcium concentration, of which there are 3 generally recognized causes. These are excess of sodium or potassium, low total calcium and alkalosis. When there are other evidences of tetany and when the symptoms suggestive of cerebral injury or atelectasis clear up after calcium therapy, he suggests that tetany is probably the causative factor.

**THRUSH.**—Evidence to support the causal relationship of certain fungi of the *Monilia* (Castellani) group to vaginitis and to oral thrush has been contributed by H. C. Hesseltine, I. C. Borts, and E. D. Plass (Am. J. Obst. and Gynec. 27: 112 (Jan.) 1934). Pure cultures of fungi were introduced into fungus-free vaginas of pregnant and nonpregnant women. In a high percentage of instances a vaginitis resulted and the same organism which was used for inoculation was recovered. Likewise, pure cultures of *monilia* were introduced into fungus-free mouths of newly-born infants. Typical clinical thrush followed and the inoculating organism was again recovered. The authors consider this

satisfactory evidence to postulate that direct contamination of the mouth with the vaginal discharges during or shortly after birth is an acceptable explanation for certain sporadic cases of thrush.

### **PNEUMONIA IN INFANCY AND CHILDHOOD.—*Etiology.* —**

*Newborn*—A study of pneumonia in newly-born and stillborn infants with an attempt to determine the etiological factors has been made by Margaret Warwick (Am J M. Sc. 187·253 (Feb ) 1934). In 240 consecutive necropsies upon infants, stillborn or dying during the first week of life, 43 had pneumonia. Of these, 55·7 per cent. lived less than 2 days. Since pneumonia could scarcely develop in less than 2 days, it may be concluded that the onset was *in utero* in certain instances. It is noteworthy that pneumonia was present in 3 infants delivered by Cesarean section. Because the majority of the infants had physical handicaps, it was concluded that lowered resistance might be a contributing factor to the pulmonic involvement. While the author was unable definitely to determine the exciting cause of the pneumonia, it seemed to rest between aspiration of a bacterially contaminated amniotic fluid and aspiration of a sterile irritating amniotic fluid, particularly when it contains large amounts of bile and cornified epithelial cells. Her evidence seems to favor the latter.

*Bacillus Mucosus Capsulatus*—Two cases of bronchopneumonia in infancy caused by *Bacillus mucosus capsulatus* are reported by J. A. Ferguson and A. T. Tower (Am J Dis Child 46·59 (July) 1933). The patients were 7-months-old twins. One of them died and the other recovered after a hospitalization of 32 days. *Bacillus mucosus capsulatus* was recovered from the lungs at autopsy in the first instance and in practically pure culture from the nose and throat in the second. While there is no way to make an exact diagnosis of pneumonia due to this organism during life, the authors suggest that a positive throat and tracheal secretion culture from a patient with pneumonia who exhibits extreme pallor, dehydration and mucopurulent nasal discharge is strong evidence for it. X-ray findings which are described as typical of pneumonia due to the *B. mucosus capsulatus* in adults were not present in these infants.

**Treatment.**—*Serum Therapy*—A study of the effect of serum on the course and mortality of pneumonia in children is being carried on by C. Kereszturi and D. Hauptman (J. Pediat. 4·331 (Mar.) 1934). While the number of cases in their series to date is too small to permit statistical evaluation, they do have some interesting data. The difference in the death rate between the serum treated and nonserum treated cases was not significant. However, the duration of the illness seemed to be decreased in the serum treated cases. Thus, the average duration of pneumonia without serum treatment was 10 days, when serum was given intramuscularly, 9 days, and when the serum was given intravenously, 8 days. In their experience, as in that with adults, Type I pneumonia seemed to respond best to serum treatment. The most frequent types of pneumococci in their series were XIV, XIX, I and VI. Pneumococci were obtained either from throat swabs or from lung suction or from both. In their hands the lung suction method was not a more accurate means for securing the pneumococci than the throat swab method.

The low mortality of lobar pneumonia in children and the frequency of mixed infections in bronchopneumonia are only two of the obstacles in such a study as this. In the authors' words, "the multiplicity of pneumococcus types, the difficulty in obtaining potent serums for a variety of types, the necessity of the administration of serum at an early stage of the pneumonia, and finally, the careful attempt to avoid serum sickness and serum shock, makes this research a difficult and time-consuming piece of work. It is evident that potent serum for at least the dominant types must be provided, and that many more cases must be treated before a final conclusion can be reached as to the practical value of the serums in the pneumonias due to the different types of pneumococci"

R. L. Nemir (*Ibid* 3:827 (Dec.) 1933) has also studied the effect of anti-pneumococcus serum upon the course of pneumonia in children. Serum was given to 82 of 207 patients with lobar and bronchopneumonia. The mortality rate for the combined group of patients with lobar and bronchopneumonia who received serum was lower than for those who did not receive serum, although the author states that a much larger group of cases is necessary before deductions can be drawn. The duration of lobar pneumonia was definitely shortened in the group who received serum. The most striking results were obtained with antipneumococcus Types I and XIV serum. The former is the predominant type for children and the latter for infants. Of the 109 children in the serum and control group of lobar pneumonias, 72 were infected with Types I and XIV pneumococci.

*Oxygen and Carbon Dioxide Therapy.*—A study to determine the advantages and shortcomings of a simple form of oxygen tent (Guedel), a small canvas hood fitting over the patient's head, supplied with oxygen through an opening at the top, has been conducted by G. Lubin and J. G. M. Bullowa (*Am J Dis Child* 46:322 (Aug.) 1933). Because of the increased use of oxygen and oxygen and CO<sub>2</sub> therapy it seems worth while to quote verbatim the conclusions of these writers, which are as follows:

"1. Canvas is not a suitable material to confine oxygen because when the tent is dry it is too porous; it fails to confine oxygen but confines body heat. Sealing the pores with water increases the retention of oxygen, but also causes an increase in the humidity and heat retention.

"2. A tent which depends for the circulation of air on the currents produced by oxygen entering from an aperture on the top is unsatisfactory because of the insufficient circulation of air.

"3. The use of a fan for cooling by evaporation from a canvas tent is an inadvisable procedure because the rate of depletion of oxygen is increased unless the tent is continuously wet."

**POLIOMYELITIS.\*—Definition.**—F. M. R. Walshe (*Brit M J* 2:119 (Dec. 30) 1933) defines poliomyelitis as a small group of infections of the nervous system due to the action of ultramicroscopic viruses, the morphological identities of which are unknown.

**Etiology.**—(a) **PREDISPOSING CAUSES—Blood Group.**—According to the studies of K. Hatzkey (*Munchen med. Wchnschr* 80:1973 (Dec. 15) 1933), the various blood groups exert no predisposing influence in poliomyelitis.

\* See also Section on NEUROLOGY



*Age.*—Eighty-three per cent. of the 269 cases of poliomyelitis reported in California during the first 5 months of 1934 (J. A. M. A. 102:2029 (June 16) 1934) were under the age of 15 years (from 1 to 4 years, 28 per cent.; from 5 to 9 years, 38 per cent.; from 10 to 14 years, 17 per cent.). In the series of 144 cases reported by K. Blanchard (M. Rec. 139:385 (Apr. 18) 1934) 44 per cent. occurred in children under 5 years of age; 56 per cent. were 5 years or over. The term "infantile paralysis," according to the author, is a misnomer, as poliomyelitis is a disease of childhood rather than of infancy.

The cause of the relative infrequency of poliomyelitis in adults is not well understood, although it is generally believed to be due to immunity derived from abortive or subclinical forms of the disease. In West Africa, according to N. P. Hudson and E. H. Lennette (Am. J. Hyg. 17:581 (May) 1933), poliomyelitis occurs sporadically. In Liberia, the blood of 20 adults, little exposed to whites, was examined for the property of virus neutralization. Eighteen specimens neutralized the virus, 1 failed, and 1 monkey died of intercurrent infection. The proper interpretation of these findings, the authors state, depends entirely on the significance of the neutralization test as a specific immune reaction.

J. R. Paul and J. D. Trask (Tr. A. Am. Physicians 48:23, 1933) observed that with the *passage* strain of virus, the presence of antiviral seems rather to be an expression of age in that the majority of children under 10 years of age failed to show neutralization, regardless of whether they had sustained either a frank or an abortive attack of the disease. Above this age, although the results are difficult to interpret, there was some relationship to the clinical attack. There is much to be learned about the normal amounts of neutralization antibodies for human strains of the virus, and their rate of increase and decline following an acute attack of poliomyelitis. Nevertheless, the authors state that an increase of antibodies, which completely or partially neutralizes the virus, appears in the blood shortly after the mild, abortive attacks of poliomyelitis.

*Maturity* alone, according to the studies of N. P. Hudson, E. H. Lennette, and E. Q. King (J. Exper. Med. 59:543 (May) 1934) is not responsible for the virucidal property of serum. From their studies with adult *rhesus* monkeys and sub-adult *chimpanzees*, C. W. Jungeblut and E. T. Engle (*Ibid.* 59:43 (Jan.) 1934) conclude that maturity alone, whether naturally or artificially produced, conveys to the animal a certain degree of enhanced resistance, which in all probability is purely physiological. This enhanced resistance apparently manifests itself chiefly in the liberation of preformed virucidal antibodies into the serum of the prepared animal, elevating the neutralizing substances from an imperceptible level to a recognizable one. Quite apart from the physiological resistance to infection, the authors state that a proportionately higher degree of protection may be obtained by immunization with the specific virus. Both processes, although accomplishing similar results, are obviously totally dissimilar in mechanism.

*Season*—From January to July, 1934, inclusive, 2266 cases of poliomyelitis were reported in California. The epidemic apparently reached its peak during the month of June with the report of 1192 cases of the disease.

*Anatomical Factor.*—*Anthropometric Characteristics*—H. E. Thelander and H. B. Pryor (Arch. Pediat. 50:749 (Nov.) 1933) examined 100 paralyzed

poliomyelitis patients and 518 normal controls by anthropometric measurements. When the individuals of the two groups were compared according to age and sex, no differences in anatomical characteristics were demonstrated with the exception of those readily explained as the result of the disease. Morphological characteristics compared by observational methods show no consistent outstanding difference between the two groups, with the possible exception of predominance of a high, narrow palate in the poliomyelitic children. Even with extensive atrophy of muscles and bone due to paralysis, no difference in subcutaneous tissue could be demonstrated between the paralyzed limb and the nonparalyzed mate, when measured by subcutaneous tissue calipers.

(b) SPECIFIC CAUSE.—From a review of the literature, P. H. Harmon (Am. J. Dis. Child. 47: 1179 (June) 1934) contends that while conclusive evidence in favor of a filtrable virus as the etiologic agent of poliomyelitis has not been produced to the satisfaction of all, the data are overwhelmingly in favor of this assumption. Recent investigation, according to Harmon, has failed to support the view of Flexner, Noguchi and Amoss that *globoid* bodies represent the active agent. The proponents of the streptococcus etiology of the disease have not been able to marshal significant additional evidence to support their claims. On the other hand, in animal experimentation with the virus the disease has been reproduced so easily and regularly that grave doubt is cast on the irregular and questionable results obtained with the other agents.

*Louping-ill* and its similarity to acute anterior poliomyelitis has been discussed by W. S. Gordon (Brit. M. J. 1: 885 (May 19) 1934). *Louping-ill* is an encephalomyelitis of sheep caused by a tick-borne, filtrable virus. Invasion of the central nervous system occurs late in the disease and in many cases does not take place at all. Such abortive types of the disease can be diagnosed by the detection of virus in the blood, drawn at an early stage of the febrile reaction. From a comparative point of view, the author points out that in the early stage of poliomyelitis, the specific virus may be present in the blood. If such early blood infection were demonstrated, present views regarding the nature of poliomyelitis infection and its prevention and treatment, would require revision.

**Transmission.**—*Mosquitoes*—Under conditions of the experiments of J. S. Simmons, R. A. Kelser and V. H. Cornell (Proc. Soc. Exper. Biol. and Med. 31: 496 (Jan.) 1934), the mosquito *Aedes aegypti* failed to transmit the virus of poliomyelitis from infected to normal monkeys. The authors, however, believe that the general subject of insect transmission of poliomyelitis deserves further study.

**Portal of Entry.**—From experimental observations J. A. Toomey (Proc. Soc. Exper. Biol. and Med. 31: 680 (Mar.) 1934) states that failure to produce poliomyelitis after the virus has been introduced into the gastrointestinal tract perhaps may have been due to the fact that the virus did not approximate the gray fibers for which it has a particular affinity. Consequently, the abdominal cavities of 2 monkeys were opened and a short segment of the small intestine just above the cecum was grasped between 2 intestinal clamps. A 1 per cent. emulsion of virus was injected through a needle into the isolated segment, tensely dilating it.

The clamps were removed when the pinch reflex disappeared and the wound was closed. Both animals developed poliomyelitis.

Because of the remote possibility that this emulsion had been regurgitated and that the infection had taken place through the olfactory tracts, the experiment was repeated. This time the injections were made subserosally instead of into the lumen of the bowel. Poliomyelitis occurred in both animals.

*Olfactory Nerves*—E. W. Schultz and L. P. Gebhardt (*Ibid* 31:728 (Mar) 1934) cauterized the olfactory nerves and bulbs of 6 monkeys through openings made in the frontal bones at the level of the olfactory bulbs. After convalescence, these animals with 3 control monkeys were inoculated intranasally with the poliomyelitis virus; only the control animals developed the disease. The inoculations were repeated, again, the control monkeys alone developed poliomyelitis. Three weeks later the operated animals were injected intracerebrally with poliomyelitis virus; all developed poliomyelitis.

The results of these experiments, according to the authors, strongly support the view that the virus normally passes from nasal mucous membranes to the central nervous system by way of the olfactory nerve, olfactory bulb and olfactory tracts. Only in so far as the cauterization may have destroyed possible vascular communication does this evidence lack finality.

Whether the olfactory nerve affords the virus a passage because it is non-medullated, or because its neurones lie in the nasal mucosa and are thus exposed to the virus is not known. The fact that injection *via* the sciatic nerve succeeds only if the nerve is injured, and inasmuch as injury to the nerve is followed by myelin degeneration, suggests that the lack of myelin may render the olfactory nerve vulnerable to the virus.

*SPREAD OF VIRUS*—J. A. Toomey (*Ibid* 31:702 (Mar) 1934) demonstrated that in cord-transected animals, transfer of the virus can occur from the upper to the lower part of the cord after intercerebral injections of the poliomyelitis virus, as well as from the lower to the upper part of the cord after sciatic injection. Presumably the virus is disseminated along the sympathetic nerve fiber connections.

The results obtained by M. Brodie and A. R. Elvidge (*Science* 79:235 (Mar 9) 1934) are in contrast to those of Toomey (*loc. cit.*). Brodie and Elvidge separated the cord of monkeys in the dorsal region, at the same time preserving the normal flow of cerebrospinal fluid. Virus inoculated into the brain failed to infect the lower segment, conversely, virus inoculated into the lower segment did not pass beyond the section of separation. According to the authors, these results show that the spread of the virus through the central nervous system is along nerve tracts rather than by means of the cerebrospinal fluid. Inasmuch as the perineural lymph spaces of the olfactory nerve continue as the subarachnoid spaces and the nerve fibers continue in the central nervous system, the virus must travel along the fibers of the nerves. It is also emphasized that the spread of the virus in the nervous system is not hematogenous, since the blood supply was intact for each segment.

*Pathology*.—T. B. Quigley (*J. A. M. A.* 102:752 (Mar 10) 1934) observed that 75 per cent of 81 fatal cases of poliomyelitis had a mild hemorrhagic

gastritis at necropsy; 86.7 per cent. had a definite hyperplasia and congestion of the lymphoid tissue. The average weight of the thymus in poliomyelitis was usually from 10 to 15 per cent. greater than the average normal weight. While the greater part of the hyperplasia was thought to be a manifestation of the disease, the fact that in more than 30 per cent. of the series the faucial tonsils had been removed, suggests, according to the author, that some degree of constitutional lymphoid hyperplasia exists in some cases. (However, it should be pointed out that tonsillectomy has occasionally been considered a predisposing cause of poliomyelitis.)

The pale, muddy, granular appearance of the cut surface of the liver of those dying of poliomyelitis, Quigley (*loc. cit.*) felt to be almost peculiar to the disease. The appearance of the liver was found to be quite distinct from the diffuse, cloudy swelling encountered in most infectious diseases, but had no specific microscopic characteristics.

Changes in the central nervous system of a patient during a relapse of poliomyelitis, illustrated, according to the author, the often observed lack of correlation between clinical and pathological observations. No involvement of the extremities was apparent in the second attack, yet marked nerve cell degeneration, neuronophagia, congestion and edema were found at every level of the cord examined postmortem.

M Brodie (J. Immunol. 25:71 (July) 1933) observed an unequal and irregular distribution of virus throughout the cerebrospinal axis of monkeys, as demonstrated by the high infectivity of the cord, medulla and pons, as compared to the midbrain, cerebrum and cerebellum. At the acute stage of the disease in monkeys, there is a relationship between the infectivity and the amount of nerve cell destruction of the various areas of the cerebrospinal axes.

The *sympathetic* nervous system, according to studies made with autonomic drugs by J. A. Toomey (Am. J. Dis. Child. 47:573 (Mar.) 1934), is involved in a segmental fashion just as early as the somatic system.

The *capillaries* of 19 children with infantile paralysis were studied by A. Fiorentini and A. Jemma (Riv. di clin. pediat. 30 1171 (Sept.) 1932). In the early weeks of the paralysis there was an increase in the number of capillaries, associated with redness of the skin. After several weeks the number decreased. One or more years after the paralysis, although there was some dilatation, the capillaries were still fewer in number, apparently resulting from diminished circulation of the atrophied muscles. Examination of capillaries does not seem to be of prognostic value in regard to recovery from paralysis.

**Symptomatology.**—M. B. Brahdry and M. Lenarsky (J. A. M. A. 102 1358 (Apr. 28) 1934), in their study of poliomyelitis, recognize the generally accepted 3-phase course of the disease. The first stage is the general invasion or systemic phase, the second, the meningitic phase, with symptoms of central nervous system involvement. The third stage is the preparalytic (Chart I).

In the dromedary course of the disease, there is a latent interval of well-being between the first and second stages.

Four variations in the clinical course of the dromedary type have long been recognized, *i. e.*, those in which the latent, or symptom-free, period is absent—the

straggling type; those in which the first phase is absent—the sudden onset type; those in which the second and third phases are absent—the abortive form; and those in which the third phase is absent—the nonparalytic type

The opinion that the course of the disease can be divided into the 3 phases is now challenged, according to F. M. R. Walshe (Brit. M. J. 2: 1197 (Dec. 30) 1933), by workers in the problems of poliomyelitis S. D. Kramer and G. C. Parker (Proc. Soc. Exper. Biol and Med 30: 1417 (June) 1933) observed evidence of involvement of the nervous systems of monkeys as early as the third day following the first intranasal instillation, at least 2 days before the appearance of fever, and 5 days before the appearance of paralysis

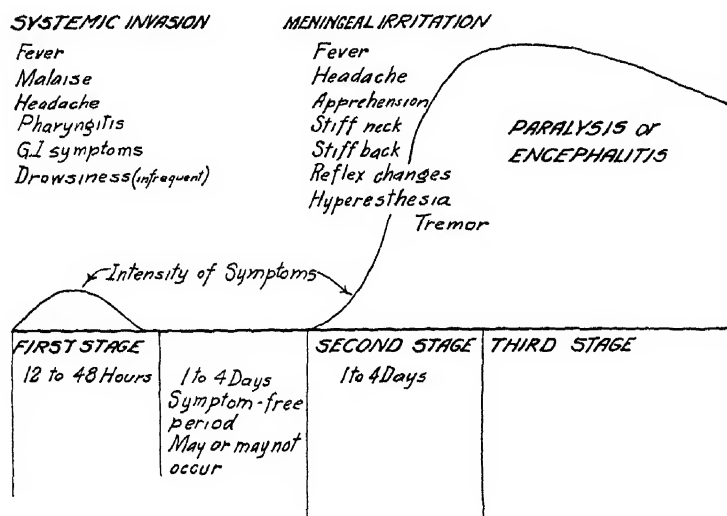


Chart I—Clinical course of poliomyelitis (Brahdy and Lenarsky J. A. M. A.)

The initial or systemic stage, Walshe (*loc. cit.*) states, does not exist, poliomyelitis from the beginning is primarily and exclusively an infection of the nervous system. Manifestations of meningitis are late rather than early findings; the attack upon the nerve cell has begun before diagnosis is possible. Apparently, there is no clinically recognizable stage in which the nerve cell is intact and free from infection. Consequently, there are only paralyzed and nonparalyzed cases. The clinical distinction cannot be made by dividing cases into the *abortive* type, in which only the systemic phase exists, and the nonparalytic type, in which meningeal involvement occurs with damage to the nerve cells.

On the other hand, J. P. Martin (Brit. M. J. 2: 1200, 1933) contends that the disease ordinarily consists of both a *general* or *systemic* and a *nervous* system infection, furthermore, in the majority of infected persons the nervous system is not involved. As evidence of a systemic invasion, the author emphasizes the occurrence of a general lymphoid hyperplasia in poliomyelitis. The virus, too, has been found in the mesenteric lymph node. Again, immune bodies are found in the blood stream after an attack of the disease.

Granting that the nervous system usually becomes infected directly from the nasopharynx by way of the olfactory nerve, the nervous system infection can no longer be regarded as secondary to the general systemic invasion; it must occur

more or less concurrent with it. The time relation between the two probably varies from case to case, for once the virus becomes localized in the nasopharynx, several varieties or combinations of infections are possible.

1. General blood infection without nervous system involvement.

- 2 If the nervous system is attacked by way of the olfactory nerves, blood stream invasion from the nasopharynx may occur simultaneously with, before, or after invasion of the nervous system.

- 3 The virus may infect the nervous system without blood stream invasion; the general infection then probably occurs secondarily and late.

**Cerebrospinal Fluid.**—The spinal fluid during the systemic phase, K Blanchard (M. Rec. 139:385 (Apr. 18) 1934) states, is normal, but a second lumbar tap when the neck and spine become rigid will show the characteristic findings.

The *appearance* of the fluid ranges from water clear to that of ground glass. Brahdy and Lenarsky (*loc cit*) have occasionally encountered turbid fluid. The *globulin* content, according to Blanchard, is usually increased. The *pressure* is usually slightly elevated; the amount of fluid required to be removed until the pressure drops, varies from 25 to 45 c.c.

The *cell count* of the spinal fluid in the cases studied by Blanchard (*loc cit.*) was maximal during the preparalytic stage, and dropped as paralysis set in. The cell count, according to Brahdy and Lenarsky (*loc. cit*) is usually increased if the examination is made early in the stage of paralysis; occasionally, the cell count is within normal limits. When the puncture is made late in the paralytic stage, the spinal fluid is frequently normal. P. H. Harmon (Am. J. Dis Child 47:1216 (June) 1934) states that while it is true that the average of cell counts for patients who were never paralyzed is lower than the average cell count in fatal cases, the difference is not striking.

In the majority of cases, as Brahdy and Lenarsky (*loc cit*) point out, the cell count is less than 300 per c.c., although the authors have encountered one patient with a count of 1640 cells and Blanchard (*loc cit.*) a patient with a spinal fluid count of 1500 cells per c.c. Of the group of 144 cases studied by Blanchard, 85 per cent had cell counts below 200 per c.c.; 35 below 50 per c.c. In only a few of the patients was the count greater than 200 c.c. Of the bulbar cases, in which there was no apparent involvement of the cord at all, 10 patients had a count below 100 and the others varied from 102 to 538. The neutrophilic polymorphonuclear leukocytes were most common in the early stages of poliomyelitis, but soon the lymphocytes predominated almost to the exclusion of the polymorphonuclear leukocytes, even in the preparalytic stage.

The *sugar* content of the spinal fluid, Brahdy and Lenarsky state, is usually normal, may be low, but is never absent. A. Ghio and A. Ranno (Riv. di clin. pediat. 30:1159 (Sept.) 1932), on the other hand, have found that the glucose content tends to be higher than normal, particularly was this true in the bulbar form of the disease.

**Diagnosis.**—The diagnosis, Blanchard (*loc cit*) states, is based upon clinical as well as laboratory data, but in an epidemic the latter is more reliable. Of 144 cases studied, 20, upon admission, presented only a slight rise in temperature,

with few constitutional symptoms, and with no physical findings suggestive of poliomyelitis. Upon spinal puncture, the characteristic findings of poliomyelitis were observed. Three of the 20 patients developed paralysis.

*Ebersson Colloidal Gold Test.*—The colloidal gold test for the detection of poliomyelitic antibodies in serum did not enable E. W. Schultz, C. E. Clifton, L. P. Gebhardt and J. V. Chambers (J. Immunol. 26:119 (Feb) 1934) to distinguish between serums collected from poliomyelitic convalescent monkeys and normal monkeys. The substance in the serum which is responsible for the phenomenon seems to fluctuate in amount and may be closely related to food stuffs ingested and absorbed.

*Differential Diagnosis.*—If poliomyelitis is considered as occurring in 3 stages, Brahdy and Lenarsky (*loc. cit.*) contend that the differential diagnosis will be simpler and the percentage of incorrect diagnoses will decrease. There is a tendency, especially during epidemic periods, the authors contend, to make the diagnosis of poliomyelitis without obtaining a history and making a careful physical examination. As the disease progresses into the second and third stage, there are more tangible symptoms on which to make a positive diagnosis. Parallel with the increase in the number of symptoms there is an increase in the number of conditions mistaken for poliomyelitis.

In a group of 2700 cases analyzed by J. F. Landon (J. Pediat. 5:16 (July) 1934) who were admitted to hospitals for poliomyelitis, the diagnosis was not verified in 300 patients. In general, in addition to respiratory infections, the rejected cases naturally fell into 2 groups: (1) those exhibiting evidence of involvement of the central nervous system without demonstrable paralysis, and (2) those manifesting paralysis or pseudoparalysis.

In the first group were found patients with (a) tuberculous meningitis; (b) meningococcic, pneumococcic, streptococcic and other forms of pyogenic meningitis, (c) meningismus; (d) acute rheumatic fever, (e) rheumatic torticollis, (f) sepsis, (g) acute appendicitis, (h) tetanus.

In the second group were cases of (a) peripheral neuritis, due to chronic alcoholism, lead, arsenic, mercury poisoning, etc.; (b) injury or infection of the bones, joints or muscles, (c) hysteria, (d) facial paralysis, (e) transverse myelitis.

Of 1123 patients admitted to the Willard Parker Hospital in 1931 with the diagnosis of poliomyelitis, Brahdy and Lenarsky (*loc. cit.*) found 113 did not have the disease. Thirty-six other conditions were diagnosed in the group of 113 patients. In the table on page 713 the diseases and cases are listed according to the stage of poliomyelitis which they resembled.

*Complications and Sequela.*—*Spastic Paralysis.*—D. Sashin and D. Arbuse (Arch. Pediat. 51:40 (Jan) 1934) observed a case of irregularly disseminated spasticity of the muscles of the lower limbs and right upper extremity which developed 13 years after the onset of anterior poliomyelitis. It is thought that the pathologic process is most probably degenerative in nature, superimposed on an old poliomyelitis.

*Choked Discs.*—J. B. Ayer and L. D. Trevett (Arch. Neurol. and Psychiat. 31:396 (Feb) 1934) observed a patient with poliomyelitis with a prolonged

period of increased intracranial pressure and persistent headache lasting over a period of 5 months. In the fourth week of the illness the patient developed bilateral choked discs. The patient was thought to have had a relapse of poliomyelitis during the fifth week of the illness.

TABLE I  
ONE HUNDRED AND THIRTEEN CASES REFERRED TO THE WILLARD PARKER HOSPITAL  
WITH THE DIAGNOSIS OF POLIOMYELITIS, LISTED ACCORDING TO THE  
STAGES OF POLIOMYELITIS WHICH THEY SIMULATED

Condition	Cases	Stage of Poliomyelitis Simulated		
		I	II	III
Pharyngitis . . . . .	16	8	7	1
Gastroenteritis . . . . .	14	6	6	2
Pneumonia . . . . .	9	2	4	3
No diagnosis . . . . .	7	2	5	..
Tonsillitis . . . . .	7	3	4	..
Tuberculous meningitis . . . . .	5	.	4	1
Injury . . . . .	6	1	2	3
Hysteria . . . . .	4	.	2	2
Cerebral hemorrhage or arteriosclerosis . . . . .	4	.	1	3
Cerebrospinal meningitis . . . . .	4	.	2	2
Epiphysitis or arthritis . . . . .	3	.	.	3
Rheumatic fever . . . . .	3	.	3	.
Otitis media . . . . .	2	2	.	.
Serum reaction . . . . .	2	2	.	..
Torticollis . . . . .	2	.	2	.
Neuritis . . . . .	2	.	.	2
Osteomyelitis . . . . .	2	1	1	..
Grip . . . . .	2	1	1	.
Synovitis . . . . .	2	.	.	2
Myositis . . . . .	1	..	1	.
Adenitis . . . . .	1	.	1	.
Congenital syphilis . . . . .	1	.	.	1
Abscess . . . . .	1	.	1	.
Typhoid . . . . .	1	1	.	.
Tetanus . . . . .	1	.	.	1
Vaccination . . . . .	1	.	1	.
Bell's palsy . . . . .	1	.	.	1
Epilepsy . . . . .	1	.	.	1
Encephalitis . . . . .	1	.	.	1
Cellulitis . . . . .	1	.	.	1
Focal myelitis . . . . .	1	.	.	1
Subperiosteal abscess . . . . .	1	.	.	1
Purpura with arthritis . . . . .	1	.	1	..
Transient contractures of unknown origin . . . . .	1	.	1	..
Acute appendicitis . . . . .	1	.	1	.
Epidural abscess . . . . .	1	..	.	1
Total	113	28	50	35

*Osteoperiostitis*.—L. Babonneix and A. Miget (Bull. Soc. de pédiat. de Paris 30:25 (Jan.) 1932) observed a child with osteoperiostitis of the left humerus which developed 2 years after the arm had been involved during an attack of poliomyelitis. It is thought that poliomyelitis may predispose to other pathologic processes.

*Second Attacks*.—T. B. Quigley (J. A. M. A. 102:752 (Mar 10) 1934) reported the case of a boy, aged 18 years, who developed a paralysis of both



extremities, followed by apparent convalescence for 5 weeks. Respiratory difficulty then developed and death occurred on the forty-ninth day.

Quigley (*Ibid*) states that 14 cases of second attacks of poliomyelitis have been recorded in the literature. These attacks must be distinguished from relapses which the author thinks occur relatively frequently in every epidemic. Of the 14 cases of reported second attacks, 11 are considered to be reasonably definite. According to the author, since the active virus has been demonstrated in the nasal washings of patients 7 months after the acute attack, every apparent second attack occurring within that time must be considered a relapse or recurrence. Invariably, according to G. F. Still (*Arch Dis Childhood* 5: 295 (Oct.) 1930), these relapses take place within 3 months. According to Quigley, it is characteristic of most human relapses that the exacerbation is much more severe than the original attack. The interval between the longest reported relapse and the earliest true recurrence is 2 years.

**Prognosis.**—The gravity of poliomyelitis, P. H. Harmon (*Am J Dis Child* 47: 1216 (June) 1934) states, is attested by an average mortality of from 10 to 15 per cent. Not the least to be considered is the social disability of residual paralysis, more severe grades of which occur in from 25 to 50 per cent of the cases in certain epidemics. All observers agree that the outcome of both an individual case and the given epidemic is practically impossible to predict. From an analysis of the literature, the author states that the fatality rate in the age group beyond 15 years is greater than in any hemidecade before this age for both epidemic and endemic poliomyelitis. The limited data available indicate that the more severe grades of paralysis have a tendency to occur in the first decade of life. At present, there are no data available for measuring the effect of age on the possibility of recovery from extensive paralysis.

**Prophylaxis.**—The third conference of the International Association of Preventive Pediatrics (*J A M A* 102: 2216 (June 30) 1934) concluded that in case of epidemics the following measures should be applied:

1. Compulsory notification of the disease, including sporadic cases.
2. The organization of the crusade should be intrusted to a medical service specially created for the purpose, under the charge of a qualified physician who outlines the prophylactic measures to be introduced and directs their application. The physician in charge should collect all items of information gathered in the infected area, with a view to their future scientific utilization. The physician should also attach to himself a number of competent physicians and should offer the service of this body to the medical corps to aid in the detection of cases and the application of treatment, including prophylaxis.
3. The first measure is the early detection and isolation of all cases under the best possible conditions. Provisions should be made for concurrent and terminal disinfection.
4. All necessary measures should be taken to prevent dissemination of the disease by water, milk and foods; special attention should be given to the supervision of commerce in food products.
5. Since in epidemics the infection appears to extend to the major part of the population, it is recommended that specific seroprophyllaxis be studied and possibly applied in some form that the present status of science places at our disposal. It is advisable that large supplies of convalescent serum, and possibly of other specific serums be kept on hand in established centers.
6. Carriers are apparently numerous in the infected area. Consequently, public assemblages of all kinds that might bring about a contact of persons of other regions with the

TABLE II  
EFFECT OF AGE ON MORTALITY FROM ACUTE POLIOMYELITIS (Harmon *loc cit*)

Author	Type	Epidemic	Age Groups												All Ages		
			0 to 4 Years			5 to 9 Years			10 to 14 Years			15 Years or Older					
			Num-ber of Cases	Deaths Num-ber	Per Cent	Num-ber of Cases	Deaths Num-ber	Per Cent	Num-ber of Cases	Deaths Num-ber	Per Cent	Num-ber of Cases	Deaths Num-ber	Per Cent	Num-ber of Cases	Deaths Num-ber	Per Cent
Nicoll	Pts not treated with serum	New York State, 1916	8,317*	2,362	28.4	2,319	601	25.9	531	138	26.0	515	212	41.1	11,682	3,313	29.2
Rosenow and Nickel	Treated with Rosenow's serum Untreated	Minnesota and Wisconsin, 1921-1925  Minnesota and Wisconsin, 1921-1925	440*	36	8.2	326	39	11.9	161	33	20.5	186	52	27.9	1,113	160	14.3
			149*	29	19.4	58	18	31.0	36	16	45.7	36	19	52.7	278	82	29.5
7th & 9th Bien Rpts of Minn State Bd. of Hlth 1916-1917 and 1920-1921	Untreated,	Minnesota, 1916 Minnesota, 1917-1920 Minnesota, 1921	397*	37	9.6	161	21	13.0	79	20	25.3	104	27	26.0	741	105	14.2
	Untreated		161 172	28 28	17.4 16.3	87 157	16 19	18.4 12.1	32 106	6 19	18.8 17.9	44 120	10 36	25.0 30.0	313 702	66 102	21.1 14.5
California State Board of Health	Endemic poliomyelitis	California, 1924	90	15	16.6	†	.	..	70	10	14.3	17	9	52.9	192	34	17.7
	Epidemic poliomyelitis	California, 1925	326	53	16.3	†	..	.	360	63	17.5	123	28	22.7	821	144	17.5
	Endemic	California, 1926	101	17	16.8	†			54	7	12.9	32	6	18.8	187	30	16.0
	Epidemic	California, 1927	441	59	13.4	†		..	629	106	16.8	232	59	25.4	1,298	224	17.3
	Endemic	California, 1928-1929							..						474	126	..
	Epidemic	California, 1930	457	39	8.6	646	31	4.8	327	23	7.0	441	64	14.5	1,903	157	8.2
	Endemic	California, 1931	78	18	23.1	105	10	9.5	50	7	14.0	57	15	26.3	292	50	16.4
Lumper, Thelan-der and Shaw	Epidemic	San Francisco, 1930	†			†			196	8	4.1	72	19	26.4	268	27	10.1

\* Age groups 0 to 5, 6 to 10, 11 to 15, and over 16 years

† Age groups 5 to 9 and 10 to 14, statistics are not individually available for these years, the figures in 10 to 14 year column include both groups

‡ Age groups 0 to 14 years, inclusive, given in 10 to 14 year age column.

inhabitants of the infected region should be prohibited; camps and vacation colonies for children from other sections should be prohibited. All movements of nomadic groups should be prohibited. These principles should be kept in mind in the movement of troops.

7 It is impossible to establish uniform rules in regard to the closing of schools, theatres and consultation centers. These matters must be regulated according to the special conditions surrounding each epidemic.

**PASSIVE IMMUNIZATION.**—During the epidemic of poliomyelitis in Philadelphia in the summer of 1932, H. C. Carpenter, J. Stokes, Jr., and I. J. Wolman (Am. J. Dis. Child 46:681 (Sept.) 1933) state that an effort was made for widespread prophylaxis against the disease by passive immunization.

In an area where the incidence of the disease was highest, 620 children under 10 years of age were given 60 c.c. of parents' whole blood intramuscularly. In this group 3 mild cases of the disease without paralysis developed, an incidence of 1 in 207, the incidence in the remaining children in the same area was 1 in 640. In a group of 721 children living outside the census area who received similar injections, 3 developed mild attacks of poliomyelitis.

At the Jewish Hospital, 266 children were given 20 to 40 c.c. of parents' serum intramuscularly. At St. Luke's Hospital, 343 children were given 20 c.c. of convalescent serum intramuscularly and at Mount Sinai Hospital, 229 were given 30 c.c. of adult blood subcutaneously. The age of these children ranged from 1 to 15 years, the majority being under 11 years. Apparently none subsequently developed poliomyelitis.

The incidence of poliomyelitis in the entire number of 2179 children apparently passively immunized against the disease was 6 cases, or 1 in 363. In the city, as a whole, the incidence of the disease was 1 in 555 children.

An undetermined group of children was given injections in institutions or by private physicians. Data were collected on 11 children of this group who developed poliomyelitis. Nine of these children had been given 50 to 60 c.c. of whole adult blood and 1 had received 8 c.c., and another 15 c.c. of convalescent serum. All injections had been made from 5 to 15 days before the onset of symptoms. In 1 child, severe paralysis of both legs developed, in another, moderate paralysis of one of the extremities; and in 2 others, slight transient weakness of one extremity. The remainder had no paralysis or weakness. There were no deaths. According to the authors, considered as a group, these children had a favorable course in comparison with the rest of the children.

Although the series of cases is small, the authors believe that the data suggest that passive immunization by means of adult or convalescent serum or blood is of value as a prophylactic measure against poliomyelitis.

**ACTIVE IMMUNIZATION**—It is apparent, according to Martin (*loc cit*), that no therapeutic measure, however efficacious, can provide adequate defense against a disease if the essence of its attack is a surprise one. The only hope of real protection against poliomyelitis lies in the attainment of a means of adequate and lasting immunity. As S. D. Kramer, M. Schaeffer and W. H. Park (J. Immunol. 27:199 (Aug.) 1934) point out, in the absence of any specific therapeutic agent, and until more is learned concerning the underlying factors which determine susceptibility, it appears reasonable that efforts should be made

to develop a safe, active immunizing agent against the disease. Any method of immunization employed in the disease must possess the virtue of complete safety. Furthermore, according to J. A. Kolmer and A. M. Rule (*Ibid.* 26: 505 (June) 1934), there is also the problem of determining the route of immunization. The work of certain investigators suggests that the skin may be capable of engendering a higher immunity response than the organs of the central nervous system.

Extending the analogy of *toxin-antitoxin* of diphtheria to *virus-serum* mixtures, Kramer, Schaeffer and Park (*loc. cit.*) state that experiments have suggested that such neutralized mixtures may possess antigenic properties. How-

TABLE III  
INCIDENCE OF NONPARALYTIC POLIOMYELITIS IN PREPARALYTIC UNTREATED  
(A) AND TREATED (B) AND (C) POLIOMYELITIS

Author	Date of Epidemic	Number of Cases	Non-Paralytic Cases	Per Cent	Population Unit, as a Whole		
					Cases	Deaths	Fatalities
(a) Zingher . . . . .	1916	14	8	57	9,023*	2,448	27 1
Draper . . . . .	1916	31	19	61	9,023*	2,448	27.1
Peabody . . . . .	1920	13	9	69	696	696	20 7
Lichtenstein . . . . .	1929	20	11	55	121*	20	16 5
Park . . . . .	1931	408	301	74	4,138*	504	12 2
Laidlaw . . . . .	1931	45	32	71	2,051†	154	7 5
Total . . . . .		531	380	71.5			
(b) Schwarz . . . . .	1916	21	9	43	See text	. . .	27.1
Peabody . . . . .	1916	51	35	69	1,927	452	23.5
Draper . . . . .	1916	41	20	49	See text	. .	27.1
Amoss and Chesney . . . . .	1916	14	11	79	See text	. .	27.1
Zingher . . . . .	1916	64	53	83	See text		27 1
Ayer . . . . .	1921-1926	92	66	72	\$	\$	\$
Aycock and Luther . . . . .	1927	106	37	35	1,189	169	14 2
Aycock <i>et al</i> . . . . .	1928	116	54	47	434	65	15 0
Macnamara . . . . .	1928	42	23	55	104	32	19 5
McEachern . . . . .	1928	74	69	93	434	49	11 3
Shaw and Thelander . . . . .	1928	19	17	89	303	80	26 4
Berry . . . . .		49	45x	92	289	27	9 3
Lomer and Shireff . . . . .	1929	115	109	95	\$	\$	\$
Shaw, Thelander and Limper . . . . .	1930	53	28	53	1,903	157	8 2
Lichtenstein . . . . .	1929	39	23	59	121	20	16 5
Park . . . . .	1931	519	357	69	4,138*	504	12 2
Laidlaw . . . . .	1931	764	593	78	2,051†	154	7 5
Levinson, McDougall and Thalhimer . . . . .	1931	65	31	48	170*	32	18 8
Total . . . . .		2,244	1,580	70 4			
(c) Rosenow . . . . .	1917	16	15	94	\$	\$	\$
Nuzum and Willy . . . . .	1917	14	13	93	535*	187	34 9
Sugg . . . . .	1924	18	13	72	65	16	24 6
Rosenow and Nickel . . . . .	1921-1925	232	188	81	\$	\$	\$
Rosenow . . . . .	1930	50	45	90	\$	\$	\$
Total . . . . .		340	274	80 6			

\* Number of deaths in the city alone

† Obtained from the following sources Poliomyelitis from 1929 to 1931, League of Nations Monthly epidemiological reports, 11.3, 1932 Personal communication to the author from E. Hjert, Medical Officer of Health, Stockholm, Stadshalsovardsmann.

Number of deaths in the state exclusive of New York City.

\$ No comparative data available.

x Includes a few cases that showed mild transitory paralysis

ever, the nature of the virus-serum combination is not definitely known. As was demonstrated by Andrewes (quoted by Kramer and his associates), the action of the specific immune serum on a virus is not a destructive but a neutralizing one. In their immunization experiments with animals, Kramer, Schaeffer and Park (*loc cit.*) used the *apparently* safe mixture of virus and serum which they found it possible and practical to prepare and standardize in large quantities. Nine of 12 animals inoculated intramuscularly and subcutaneously with the neutralized mixture developed sufficient immune substance in their blood so that 0.5 c c of the serum neutralized 10 infective doses of the virus.

However, Kolmer and Rule (*loc cit.*) believe that vaccination against diphtheria with toxin-antitoxin mixtures is not analogous to serum-virus preparations. In the former, toxin only is used and this is without danger of producing the disease, providing the mixtures are properly neutralized. The authors contend that up to the present time no method has been discovered for modifying the infectivity of the living virus to render it entirely safe for vaccination of human beings, analogous to vaccination against smallpox with the living virus of cowpox.

The virus of poliomyelitis may be altered by heat and chemical agents. Kolmer and Rule (*loc cit.*) attempted to immunize monkeys with 4 types of modified virus: (1) Chloroform treated vaccine, (2) sodium ricinoleated vaccine, (3) a heated and tricresolized vaccine, (4) and, finally, an untreated vaccine. In the dosage used, the chloroform vaccine failed to immunize when injected sub- and intracutaneously. The heat-treated vaccine also failed to immunize. Results obtained with the sodium ricinoleated vaccine were encouraging and worthy of further study, especially to show that this method of treating the virus is definitely capable of destroying or inactivating the agent. Although found to be effective in monkeys, multiple intracutaneous injections of untreated virus is too dangerous to use in human beings. The administration of living, untreated suspensions of the virus by stomach tube failed to produce any demonstrable evidence of immunity.

**Treatment** —**SERUM THERAPY** —Formerly, according to Walshe (*loc cit.*), it was assumed that the preparalytic stage was a brief period during which it might be hoped to neutralize the virus before it reached and began to attack the nerve cell. There is, according to the author, no such period. All that may be hoped for is to neutralize the virus already in the cell before the latter is damaged beyond repair. Experiments hold out little hope that this is possible. However, the author adds, it might almost be said that convalescent serum has not been given a fair trial in view of the lack of satisfactory control cases and the lack of conformity in the quantity and quality and the route of administration of serum, and the stage of the illness when the serum was administered.

P. H. Harmon (*loc cit.*) from a review of the literature, attempted to compare the results obtained in the treatment of preparalytic and early paralytic poliomyelitis with 3 types of serum, *i e.*, (1) the antistreptococcic serum of Rosenow, (2) convalescent and other known neutralizing serums from man, and (3) antiviral animal serums.

1. SERUM THERAPY IN PREPARALYTIC STAGE.—Heretofore, comparisons with patients treated in the preparalytic stage have been made either with those seen too late in the disease to receive treatment in this stage or with the average result in the population unit at large. By either of these methods the possibility that many preparalytic cases may be cases of nonparalytic poliomyelitis is eliminated from consideration in the control group.

It is seen from the data on 531 non-serum treated patients that even in epidemics of average severity a large share of patients (71.5 per cent.) in whom the disease is diagnosed in preparalytic stage by examination of the spinal fluid, never become paralyzed. Further examination of this table shows that larger

TABLE IV  
TREATMENT OF POLIOMYELITIS BY CONVALESCENT AND NORMAL HUMAN SERUMS (Zingher)  
(Quoted by Harmon: *loc. cit.*)

Type of Case	Serum used in Treatment	Number of Patients Treated	Number Becoming Paralyzed	Number Recovering Without Permanent Paralysis	Number of Deaths
Preparalytic	Convalescent	25	1	.	0
	Normal	10	1		1
Paralytic	Convalescent	88	.	5	38
	Normal	33		4	5

TABLE V  
CLINICAL USE OF CONVALESCENT AND NORMAL ADULT SERUMS (Brodie)  
(Quoted by Harmon *loc. cit.*)

Serum	Number of Patients	No Paralysis		Mild Paralysis		Severe Paralysis		Deaths	
		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Convalescent	25	20	80	2	8	3	12	1	4
Selected Adult	16	13	81.2	0	0	3	18.8	1	6.3

percentages of nonparalytic cases occur in the group of preparalytic cases only under 2 conditions, in the small number of cases (Amoss and Chesney, Shaw and Thelander, Nuzum and Willey, and Sugg) or in relatively mild epidemics (McEachern, Lomer and Shireff, Rosenow and Nichel, and Rosenow). The total number of nonparalytic cases alleged to have resulted from the administration of serum (70.4 per cent. of 2244 cases) is strikingly like the incidence of nonparalyzed patients in the untreated patients in the preparalytic stage.

(a) *Transfusion*.—I Sherman (*Am J Dis Child* 47:533 (Mar.) 1934) treated 71 patients with blood transfusion from immune donors. The amount of blood given ranged from 150 to 400 c.c. In only 1 instance was the transfusion repeated. At the time of treatment, 35 of the patients were in the preparalytic and 36 in the paralytic stage. The mortality rate was reduced in the first group to 2.8 per cent. and in the paralytic group to 11 per cent. The mortality rate was lower than in a previous series of patients treated with serum, in which the rate was 10 and 20 per cent., respectively. The total mortality rate was 7 per cent. as

TABLE VI  
TREATMENT OF PREPARALYTIC POLIOMYELITIS WITH HUMAN CONVALESCENT SERUM (Harmon *loc. cit.*)

Location and Date	Author	No of Cases	No of Deaths	Fatality Rate	No Paralysis	Per Cent	Paralysis that cleared	Per Cent	Paralysis slight but persistent	Per Cent	Paralysis severe	Per Cent	Observations on Control Cases
New York, 1916 Massachusetts, 1916	Schwarz Peabody	21 51	0 5	0 0 9 8	9 35	42 8 68 6	5	9 8	No	data	3 9	4	7 8 No controls. 69 pts treated in paralytic stage, 21 (32%) deaths
New York City, 1916	Draper	41	5	12 2	20	48 8	9	21 9	4	9 8	3	7 3	31 pts untreated in paralytic stage, 19 (61.3%) never paralyzed No controls available
New York City, 1916	Amoss and Chesney	14	2	14 3	11	78 6	Reports do not consider this		1	7 1	0	0 0	No controls available
New York City, 1916	Zinghet	64	1	1 6	53	82 8	5	7 8	5	7 8	Included in previous column		Compared preparalytic with early paralytic cases.
New York City, 1916	Ayer	92	7	7 6	66	71 7	8	8 7	11	11 9	Included in previous column		No control available.
Massachusetts, 1927	Aycock and Luther	106	1	0 9	37	34 9	No	data	62	58 5	6	5 7	"State as a whole," 1,189 cases, 14% fatality
Massachusetts, 1928	Aycock <i>et. al</i>	116	7	6 0	54	46 6	No	data	51	43 8	4	3 4	"State as a whole," 297 cases, 55 deaths (18.5% fatality).
Victoria, Australia, 1928	Macnamara	42	1	2 3	23	54 7	13	30 9	3	7 1	2	4 7	123 pts not treated with serum, 21.6% complete recovery, 8%; very severe paralysis, 48%.
Manitoba, 1928	McEachern	74	0	0 0	69	93.2	No	data	5	6 8	Included in previous column		54 pts. untreated, deaths, 6 (11%); residual paralysis, 34 (63%); complete recovery, only 14 (26.7%)
California, 1928	Shaw and Thelander	19	0	0 0	17	89 0	2	10.5	0	0 0	0	0 0	38 pts. untreated, deaths 3 (7.9%), no paralysis 0 (0%), mild paralysis, 2 (5.3%), severe paralysis, 33 (86.8%).

(b) Convalescent Serum.—Illustrated in Table VI.

TABLE VI  
TREATMENT OF PREPARALYTIC POLIOMYELITIS WITH HUMAN CONVALESCENT SERUM (Harmon: *loc. cit.*) (Continued)

Location and Date	Author	No of Cases	No. of Deaths	Fatality Rate	No Paralysis	Per Cent	Paralysis that cleared	Per Cent	Paralysis slight but persistent	Per Cent	Paralysis severe	Per Cent.	Observations on Control Cases
Ottawa, 1929 California, 1930	Lomer and Shireff Shaw <i>et al</i>	115 53	1 1	0 9 1 9	109 28	94 9 52 8	No	data	2 7	1 7 13.2	3 1	2 6 1 9	No controls "State as a whole," 1,903 cases; 157 deaths (8.2%).
Stockholm, 1929	Lichtenstein	39	1	2 6	23	58 9	7	17 9	8	20 5	Included in previous column		20 preparalytic and untreated patients; never paralyzed, 11 (55%); paralysis that cleared, 5 (25%); remained paralyzed, 4 (20%).
New York City, 1931	Park	519	20	3 8	357	68 8	40	7.7	102	19.6	Included in previous column		408 preparalytic patients; died, 4 (0.9%); no paralysis, 301 (73.7%); weakness only, 58 (14.2%); paralysis, 45 (11%).
New York, 1931	Laidlaw	689	24	3 5	533	77 4	85	12 3	47	6 8	Included in previous column		None given; average outcome in the state, exclusive of New York City, 2,051 cases; 164 deaths (8%).
Chicago, 1931	Levinson <i>et al</i>	65*	3	4 5	31	47 7	20	30 7	8	12 3	3	4.6	None given; average outcome in Chicago alone, 170 cases with 32 deaths (18.8%).
Montreal, 1931	Brodie	41†	2	4 9	33	80 5	No	data	2	4 8	6	14 6	None given; average outcome in the Province of Quebec, 1,114 cases with 150 deaths (13.5%).
Totals‡		2,181	81	3 7	1,508	69 1	210	13 0	150	22 6	32	4 8	

\*This number includes 33 patients treated with neutralizing serum from normal adults.

†This number includes 16 patients treated with neutralizing serum from normal adults.

‡The totals are given per item, the percentages are calculated from the corresponding data.

(c) *Rosenow's Serum* — Illustrated in Table VII.

TABLE VII  
PREPARALYTIC POLIOMYELITIS TREATED WITH ROSENOW'S SERUM (Harmon *loc cit.*)

Location and Date	Author	Num-ber of Cases	Num-ber of Deaths	Fatal-ity Rate	No Paral-ysis	Per Cent	Paral-ysis that cleared	Per Cent	Paral-ysis but per-sistent	Per Cent	Paral-ysis severe	Per Cent	Observations on Control Cases
Iowa, 1917	Rosenow	16	0	0 0	15		1		0		0		23 patients untreated; 9 deaths, 35% mortality.
Chicago, 1917	Nuzum and Willy	14	1	7 1	13		0		0		0		100 pts. untreated, 38 deaths, 38% mortality.
Iowa, 1924	Sugg	18	0	0 0	13		1		2		2		No control
Omaha, 1923	Clark and Dow	6	0	0 0	6		No data						41 pts. untreated, 9 deaths, no statistics as to extent of paralysis.
Wisconsin and Minnesota, 1921-1925	Rosenow and Nickel	269 232	8	2 9	188	81 0	Included in previous column		31	13 4	13	5 6	177 pts untreated; 31% with paralysis; others, 19% and 48.3%, respectively (see author's table); 82 of 278 died (29.5%)
Not given	Rosenow	50	2	4 0	45	90 0	2	4 0	1	2 0	0	0 0	39 pts. untreated; 7 (17.9%) with slight paralysis; others, 4 with no paralysis (10.3%); 15 (38.4%) the latter with marked paralysis; 13 of 39 died (33.3%) mortality.
Totals*		373	11	2 9	280	83 0	4	1 2	34	11 1	15	4 4	

\*The totals are given per item, the percentages are calculated from the corresponding data



compared with the grand rate of 10 per cent. There were only 3 cases of paralysis among those treated in the preparalytic stage with transfusions as compared with 50 per cent. in the group treated with convalescent serum. The author has concluded that transfusions from immune donors appear to be the method of choice in the treatment of acute poliomyelitis.

## 2. SERUM THERAPY IN PARALYTIC STAGE.—

### (a) *Convalescent Serum*.—Illustrated in Table VIII.

TABLE VIII  
TREATMENT OF EARLY PARALYTIC POLIOMYELITIS WITH HUMAN CONVALESCENT SERUM  
(Harmon: *loc. cit*)

Author	Number of Cases	Number of Deaths	Fatality Rate	Paralysis that Cleared	Per Cent.	Paralysis slight but persistent	Per Cent.	Paralysis Severe	Per Cent
Taylor . . . . .	14	0	0 0	8	57 1	6	42.8	Included in former column	11 1
Amoss and Chesney	9	0	0 0	2	22 2	6	66 6	1	11 1
Zingher . . . . .	152	50	32 9	12	7 9	94	61 8	Included in former column	10 5
Macnamara . . . .	19	0	0 0	11	57 9	6	31 6	2	10 5
Lomer and Shireff .	26	2	7 7	0	0 0	24	92 3	Degree of paralysis not stated	25 0
Shaw and Thelander	24	5	20 8	6	25 0	7	29 2	6	25 0
Shaw, Thelander and Limper. . .	39	7	17 9	9	23 1	23	58 9	..	..
McEachern <i>et al.</i>	33	11	33 3	7	21 2	15	45.5	..	..
Totals	352	82	23 3	55	17 4	43	48 8	14	16 6

E. Moody and C Hesselberg (Arch Pediat 51:11 (Jan.) 1934) used **Rosenow's serum** in the treatment of 15 patients in the paralytic stage of the disease. The authors felt that death was prevented in 1 case by the use of the serum. In this group, 13 of the children are now perfectly normal. One child with practically total voluntary muscle involvement now has paralysis of only one shoulder. One child still requires artificial aid on locomotion. One child has a slight defect easily corrected.

The data presented in the table, according to Harmon (*loc cit*), is self-explanatory. In Tables VI, VII, and IX it is consistently shown that the fatality rate is lower in the cases in which serum was given than in the control cases or among the whole group of reported cases for a given state or year, except in the data presented by Park, in which the difference between the treated and untreated patients is slight enough to be explained by chance variation. In Table VIII, the data are conflicting. In a direct comparison of the data presented for convalescent serum from man and that presented for the antistreptococcic serum of Rosenow, there is no fundamental difference, in fact, slightly better results were obtained with the latter serum. Contending that a streptococcus is not the cause of poliomyelitis, the author states that the alleged efficacy of Rosenow's serum is indirect evidence against the efficacy of convalescent serum.

Harmon (*loc. cit*) analyzed reports of 4400 cases of poliomyelitis treated with serum and compared them with 2660 in which no such treatment was

(b) *Rosenow's Serum*.—Illustrated in Table IX.

TABLE IX  
EARLY PARALYTIC POLIOMYELITIS TREATED WITH ROSENOW'S SERUM (Harmon: *loc. cit*)

Location and Date	Author	Number of Cases	Number of Deaths	Fatalty Rate	Paral- ysis that cleared	Per Cent	Paral- ysis slight but per- sistent	Per Cent extent of paralysis	Paral- ysis severe	Per Cent	Observations on Control Cases
Iowa, 1917	Rosenow	17	0	0 0	16		1				
Chicago, 1917	Nuzum and Willy	138	11	7 9	No data		given on				75 pts. untreated; 13 deaths, i.e., 17.3% mortality (this excludes 25 of 100 showing respiratory paralysis on admission).
Iowa, 1918	Rowan	66	0	0 0	No data						17 pts. untreated; 8 died; mortality, 47%.
Montana, 1921	Pease	51	2	3 9	No data						27 pts. untreated; 8 died; mortality, 29.6%.
Montana, 1922	Sippy	35	2	5 7	No data						7 pts. untreated; 2 deaths; mortality, 28.6%.
Iowa, 1924	Sugg	19	0	0 0	10		3		5		No controls
Montana, 1916	Clarke	18	1	5 5	9		3		5		State as a whole, 40% mortality.
Omaha, 1923	Clarke and Dow	11	0	0 0	11		No data	No data	No data		41 pts.; 9 deaths (untreated pts.).
Detroit	Pryer and Bernbaum	28	4	14 2	No data		given concerning		paralysis		52 pts untreated; 10 deaths; mortality 19.2%
Wisconsin and Minnesota, 1921-1925	Rosenow and Nickel	344 277	32	9 3	109	38 9	94	33 9	74	25 9	See text.
Not given	Rosenow	53	4	7 5	38	71 7	11	20 7	0	0 0	See text
Totals*		780	56	7 2	193	48 9	111	28 1	84	21 3	

\*The totals are given per item, the percentages are calculated from the corresponding data

given; the 2 series occurring coincidentally. Of the treated patients, 2637 were seen early in the disease, the majority in the preparalytic stage. The evaluation of the influence of a therapeutic agent in poliomyelitis must be, according to the author, a detailed and complex analysis which will include variable factors largely ignored until the past few years. The quality of serum given and method of administration, nature of the epidemic, the point of the epidemic curve when treatment was applied, the age of the patient and the type and degree of orthopedic after-care, etc., must be taken into consideration. The apparently favorable result when treatment is applied in the preparalytic stage is probably explained on the basis that many cases regarded as preparalytic are really non-paralytic.

#### ROUTE OF SERUM ADMINISTRATION.—

TABLE X  
COMPARISON OF EFFICACY OF METHODS OF SERUM ADMINISTRATION (Park)

Outcome*	Percentage of Cases					Died	Total	
	0	1	+	++	+++		No of Cases	Per Cent.
Intraspinal Method.								
Intraspinal-intravenous	70 0	6 7	6 7	4 4	7 8	4 4	90	100
Intraspinal-intramuscular	71 2	5 4	9 3	7 3	4 4	2 4	205	100
Intraspinal-intravenous-intramuscular	69 0	3 5	13 8	10 3	0 0	3 4	29	100
Total Per Cent. in group treated	70 7	5 5	9 0	4 9	4 9	3 1	324	100
Method Other Than Intraspinal.								
Intravenous	66 7	0 0	33 0	0 0	0 0	0 0	6	100
Intramuscular	61.9	16 6	8 3	6 0	1 2	6 0	84	100
Intravenous-intramuscular	69 8	6 4	9 5	6 3	3 2	4 8	63	100
Total of group not treated intra-spinally	65 3	11 8	9 8	5 9	2 0	5 2	153	100

\* 0 indicates no weakness, 1, weakness, +, paralysis of one muscle and ++, paralysis of several muscles, and + + +, paralysis of many muscles

In spite of total failure of statistical evidence to favor certain types of serum, *ie*, Rosenow's serum, antiviral animal serum, convalescent and "normal" serum, the rapid symptomatic response to the administration of serum cannot be totally disregarded. With the possible exception of spinal drainage, all other forms of therapy,—chemotherapy, medicinal therapy, and artificial fever—have been tried without benefit. More data are needed before it can be said conclusively that serum of any of the 4 types is totally without value. *There appears to be enough evidence from clinical observation to warrant the continued use of serums in early stages of acute poliomyelitis*

COLLECTION OF CONVALESCENT SERUM—According to P. H. Harmon (Am J. Dis. Child. 47:1179 (June) 1934), tests of serum indicate that a period of from a few months to a year after a paralytic attack is a more feasible time to obtain potent human convalescent serum than days or weeks after the acute stage. Apparently, a person having a mild attack of the disease with more or less complete recovery produces a more potent serum than either those with widespread

paralysis or those who have received serum treatment. Storage of human convalescent serum for 2 or 3 years is thought to have little effect on the concentration of the neutralizing substance. The neutralizing power of pooled normal adult serum, R. Southby and M. McKie (M. J. Australia 2:404 (Sept 23) 1933) state, appears to be between 30 and 40 per cent. of that of convalescent serum.

**DRINKER RESPIRATOR**—M. B. Brahdy and M. Lenarsky (Am. J. Dis Child. 46:705 (Oct.) 1933) divided the poliomyelitis patients with respiratory embarrassment into 2 groups, *i e.*, those with involvement of respiratory muscles and those with involvement of the bulbar centers. To this classification, N. L. Crone (New England J. Med. 210:621 (Mar. 22) 1934) adds a third group in which both mechanisms are involved. Crone as well as P. Harper and R. Tennant (Yale J. Biol. and Med. 6:31 (Oct.) 1933) agree that the respirator is of greatest value in the treatment of that group of patients whose respiratory embarrassment is due to paralysis of intercostal muscles and the diaphragm. According to Harper and Tennant (*loc. cit.*), the respirator was of little or no value in the treatment of the bulbar patients and may even have been harmful, by overcoming the coughing and choking reflex and leading to aspiration of secretions. J. F. Landon (J. Pediat. 5:1 (July) 1934) found the respirator to be of no value in bulbar cases. E. Smith and H. I. Fineberg (*Ibid.* 4:590 (May) 1934) consider the use of the respirator as definitely contraindicated in the strictly bulbar type of the disease.

**PYELITIS.—Etiology.—Anomalies**—It is becoming quite evident that anomalies of the urinary tract are important contributing factors to persistent pyuria or infection of the lower urinary tract in infants and children. That obstructive lesions may be present without a coexisting pyuria has been known from chance clinical and necropsy examinations. From the observations of J. A. Bigler (Am. J. Dis Child. 47:780 (Apr.) 1934) it would appear that anomalies of the urinary tract are not infrequent, and that the majority of them are congenital in origin. He has collected a series of 85 children with 99 anomalies of the lower urinary tract. In 69 of the children the lesion was considered to be congenital. Urinary stasis due to obstruction somewhere in the urinary tract was present in 52 instances of which 45 were due to congenital lesions. Of the 52 cases with obstruction, pyuria was present in only 26. Thus, it would appear that while urinary infection is more frequent in children with obstructive lesions than in normal children, such lesions do not necessarily lead to pyuria. When infection does take place it is exceedingly persistent, often becoming permanent, unless the obstruction is relieved. According to Bigler, catheterization or the manipulation of urologic investigation invariably results in infection when stasis is present. Thus, it must be borne in mind that a normal urine does not exclude the possibility of an obstructive lesion of the urinary tract. The table on page 723 details the nature of the lesions in this series, together with the time of diagnosis.

## ANOMALIES OF URINARY TRACT WITH AND WITHOUT PYURIA

	Number of Cases	With Pyuria Recognized		Without Pyuria Recognized	
		Ante Mortem	Only at Necropsy	Ante Mortem	Only at Necropsy
Hydronephrosis . . . . .	35	11	8	1	15
Reduplication of ureter or pelvis .	17	2	3	1	11
Obstruction of neck of bladder .	15	4	3	5	3
Calculi in urinary tract . . . .	8	5	.	1	2
Absence of hypoplasia of kidney	4	.	.	.	4
Horseshoe kidneys . . . . .	5	.	.	.	5
Cord bladder . . . . .	1	1	.	.	.
Exstrophy of bladder . . . . .	2	.	.	2	.
Ptosia of kidney . . . . .	1	1	.	.	.
Tumors . . . . .	9	.	.	9	.
Prolapse of urethra . . . . .	1	.	.	1	.
Urethral stricture . . . . .	1	.	.	1	.

**Treatment.**—A study of *urinary antiseptics in relation to fluid intake* has been made by N. F. Miller and C. C. Chu (Am J Surg. 33:457 (Mar) 1934) No attempt was made to determine the relative merits of the various urinary antiseptics used. The influence upon bacterial growth of the excreted drug from animals and humans on low and high fluid intake was measured. The authors have shown that the restriction of fluids during the time of administering antiseptic drugs definitely enhances the inhibitory effects of that drug on bacterial growth in the urine.

No attempt was made to determine the minimal amount of fluid which a patient may take with safety. They did suggest that a patient with urinary tract infection and fever is probably better treated with an adequate fluid intake until the fever has abated. They agree that urinary antiseptics are probably most efficacious in bladder infections. However, they argue that if any antiseptic is of value in cases of kidney, ureteral or urethral involvement, then its value should be enhanced by its concentration through the limitation of fluids.

In respect to the treatment of pyelitis, it is interesting to note a statement of H. F. Helmholtz (J Urol 31:173 (Feb) 1934) "From a doubter in the efficacy of **methenamine**, I have been converted to the conviction that when conditions are properly controlled it is one of the most useful urinary antiseptic substances. Comparative studies with methenamine, and with a series of the more recently widely advertised urinary antiseptics such as pyridium, hexyl-resorcinol and others, have shown successful results of treatment with methenamine after failure with other drugs . . . The most important element in the treatment with methenamine is acidification of the urine to a point at which acidity alone may play a part in inhibiting growth. At the pH of from 5.5 to 4.9, smaller doses of this drug seem to sterilize the urine. The hematuria arising from irritation caused by formaldehyde is practically always of vesical origin and is not serious in its consequences if immediately treated. By using this method of strongly acidifying the urine I have been able to use methenamine successfully in cases of acute pyelitis of early infancy, a type of case with which formerly little success could be expected."

M. F. Campbell (*Ibid.* 31:205 (Feb.) 1934) also prefers **methenamine** for the drug treatment of pyelitis in children. He computes the dose according to age, giving 10 to 12½ grains (0.6 to 0.8 Gm.) per day per annum. Thus, a 5-year-old child would receive 50 to 60 grains (3½ to 4 Gm.) per day. **Ammonium chloride** is used for acidifying the urine. The dose varies between half and equal to that of methenamine, depending upon the urinary acidity to be achieved. The drugs are given for 4 to 6 days, when a rest period of 2 to 4 days is observed, and if the urine is not then sterile, the course is repeated. If urinary sterilization does not occur within a 2 weeks' period, it is usually useless to persist longer with this treatment. The need for complete urologic examination is stressed in those instances in which cure is not obtained by medical treatment. It is emphasized that certain pre-cystoscopic data should be obtained. This includes an x-ray examination of the urinary tract for stone or spinal defects, cystography, intravenous urography and determination of the renal function by phthalein excretion and blood chemistry (nonprotein nitrogen or blood urea). If the diagnosis is not made by these means, then a cystoscopic examination with retrograde pyelography should be performed. In this connection it may be noted that in this series of 402 cases there were 16 cases of congenital posterior urethral valve, 16 cases of bladder neck obstruction; 7 cases of hypertrophy of the verumontanum; 22 cases of stricture of the urethra, of which 17 were at the meatus. **Surgical procedure**, of course, depends upon the nature of the lesion. Young children seem to withstand major urologic surgery better than adults. However, postoperative acidosis must be guarded against and an adequate water metabolism maintained. Generous **blood transfusions** are invaluable in the combat of *surgical shock*. Campbell does not attach great significance to treatment by lavage except when residuum exists. Likewise, he has not been impressed with the use of silver nitrate for pelvic lavage in cases of chronic pyelitis in children.

**KETOGENIC DIET**—In recent years Helmholz has noted that the urine from patients on a ketogenic diet frequently had bactericidal powers. A. T. Fuller (*Biochem. J.* 27:976, 1933) has shown that the principal factor inhibiting the growth of bacteria in the urine from patients receiving the ketogenic diet is *l-b*-hydroxybutyric acid, and that the activity of this substance increases in proportion to the acidity of the urine. According to Helmholz, the minimal standard of pH is 5.5 or less, and the minimal concentration of beta-hydroxybutyric acid is 0.5 per cent or greater. Methods for these determinations have been established by A. T. Osterberg and H. F. Helmholz (*J. A. M. A.* 102:1831 (June 2) 1934). Whether or not the pH value of urine is greater or less than 5.5 is determined by the use of chlorphenol test paper. This is prepared by soaking a good grade of filter paper in an aqueous solution of chlorphenol red, of a concentration of 0.04 per cent, which is then dried. This dried paper becomes yellow and is turned red in a solution of pH above 5.5. Consequently it is necessary only that the urine shall not be capable of turning the test paper red.

Inasmuch as there is no satisfactory colorimetric measure for beta-hydroxybutyric acid and since there is a fairly constant ratio between the concentration of diacetic acid and beta-hydroxybutyric acid in the urine, over a fairly wide degree

of ketosis, the authors deemed it wise to adopt a simple procedure for determining the concentration of diacetic acid and, indirectly, of beta-hydroxybutyric acid. This method is as follows:

To 800 mg. of ammonium sulphate in the ordinary Nessler comparison tube (tall form) graduated at 50 c.c. is added 3 drops of concentrated ammonium hydroxide (0.15 c.c.), 2 drops (0.10 c.c.) of a 5 per cent. solution of sodium nitroprusside, and 1 c.c. of the urine to be examined. This is allowed to stand 6 minutes at a room temperature of approximately 25° C. (77° F.). The reaction product is then quickly diluted with water to the 50 c.c. mark and mixed. This solution is immediately compared with the standard. If the color of the unknown is deeper than that of the standard, the concentration of beta-hydroxybutyric acid is greater than 0.5 per cent. If the color is lighter, the reverse is true. The standard is prepared by adding 40 c.c. of a solution, containing 2 parts of 0.04 per cent. solution of phenol red and 1.4 parts of a 0.04 per cent. solution of bromthymol blue, to 46 c.c. of phosphate buffer of pH 8.0. The standard retains its color for a considerable time, but a fresh standard may be prepared very easily if only an occasional determination is to be made.

An important factor to be borne in mind is the statement of Helmholtz (*loc cit.*) that the bactericidal power of the urine tends to disappear after 10 days of ketosis and the more rapid the production of ketosis, apparently the better the bactericidal action.

**PITUITARY EXTRACT.**—It is generally recognized that one of the requirements in the treatment of upper urinary tract infections is adequate drainage. Atony of the musculature of the kidney, pelvis and of the ureters may be an important factor in preventing this. W. Darley and W. B. Draper (J. A. M. A. 102:677 (Mar. 3) 1934) submit their own data and evidence from the literature to show that certain systemically administered drugs, such as solution of posterior pituitary extract, augment the tone and peristalsis of pelvic and ureteral musculature. The authors treated 16 patients with pyelitis, 2 of whom were children (2 and 3 years of age), with solution of pituitary. The dose was 3 and 4 minims (0.18 to 0.24 c.c.), respectively, every 6 hours—in 1 instance, for 10 days; in the other, the duration of treatment was not stated. Both patients had been fretful for some time and both became quiet shortly after treatment was begun. In all of their cases renal pain of relatively long duration was promptly relieved. The associated symptoms of fever, nausea, frequency and dysuria were also ameliorated, but in a less spectacular manner.

**RUBELLA (GERMAN MEASLES).**—Observations of serial differential counts of the leukocytes in 30 patients with rubella were made by J. V. Carroll (Lancet 1:182 (Jan. 27) 1934). He noticed a leukopenia on the first day of the rash and a slight reduction of the number of polymorphonuclear neutrophils which was most marked on the third to fifth day of the disease. The lymphocytes were increased in number, especially on the fourth or fifth day, and remained so during the patients' convalescence. At the same time the monocytes became more numerous and both monocytes and lymphocytes were frequently basophilic in appearance. The eosinophils often increased in number on the third to fifth day of the disease. Of especial interest was the appearance of relatively large numbers of plasma cells and Turck cells. The plasma cell was defined as a cell "with abundant basophil cytoplasm, with a nucleus somewhat

eccentric, which has its basichromatin concentrated to form large masses, and has a clear space to one side. The Turck cells, morphologically, came between the plasma cell and the lymphocyte. The plasma cells were noted in the blood smears of every one of the 30 patients with rubella. They usually appeared early in the disease and increased in numbers up to the third day, reaching percentages of 3 to 11. The decline in numbers occurred gradually until they had usually disappeared entirely at the end of the second week. The Turck cells were less constant in appearance and less numerous. In measles, both plasma cells and Turck cells occurred in blood smears but less frequently than in rubella. In other diseases, this type of cell was rarely found.

**SMALLPOX (VARIOLA).**—A decline in the *incidence* of smallpox in the United States and Canada during the last 3 years was reported by the Metropolitan Life Insurance Company (J. A. M. A. 101:719 (Aug. 26) 1933). The morbidity decreased 72 per cent since 1930 and the lowest incidence rate occurred in 1932. About 3 patients of every 1000 with the disease have died. In recent years, smallpox has occurred in mild epidemics in scattered parts of these 2 countries, notably in South Dakota, Vermont and Vancouver.

In severe hemorrhagic types of smallpox, the streptococcus is sometimes a secondary invader. Microorganisms of this type were isolated from the blood of 9 such patients by L. W. Fisher (J. Lab. and Clin. Med. 19:280 (Dec.) 1933). Although these bacteria bore morphologic resemblances to those of scarlet fever, erysipelas and puerperal fever, they differed in their cultural characteristics, virulence and agglutination properties. They developed a specific toxin and produced a specific antitoxin in rabbits.

**Vaccination.**—A safe and simple method of culturing vaccine virus was devised by T. M. Rivers (Tr. A. Am. Physicians 48:31, 1933). A dermal strain of vaccine virus, free from bacteria, was grown on a medium of Tyrode's solution enriched with bits of minced chicken embryo. When the potency of the virus diminished, passage through rabbits by testicular inoculation raised the virulence and cultures were again made. Some of the advantages of the cultured virus were stability and its resistance to prolonged storage, to the addition of a preservative, to freezing, and to desiccation.

Similar conclusions were reached by J. M. Coffey (Am. J. Pub. Health 24:473 (May) 1934). His preparations of vaccine material cultured in a similar manner exhibited the same characteristics of potency and stability as those of Rivers. However, in a small group of susceptible children he was unable to obtain as high a percentage of "takes" with this material as with the calf lymph.

The *optimum age* for initial vaccination against smallpox is usually considered to be 1 year. At this time of life, the percentage of "takes" is usually high and the reactions of the infant very mild or entirely absent. In communities suffering from epidemics of smallpox and where the percentage of immune persons is low, *vaccination of the newborn* was advocated by L. Isaac (Am. J. Obst. and Gynec. 27:580 (Apr.) 1934). Vaccination was performed by the multiple puncture method in 808 babies before they left the delivery room. Only 32.2 per cent of the group developed positive "takes." Reactions were generally



mild, with frequent enlargement of the regional lymph nodes, moderately severe local reactions in 8 instances and in 1 infant an ulceration and spread of the lesions. The reactions were so much more severe in premature infants than in normal ones that the procedure was not continued in that type of patient. The vaccination seemed to have no deleterious effect on the average weight gain or on the incidence of infections common to that age of life. The "takes" occurred somewhat more frequently in girls than in boys and more often in those vaccinated on the thigh than on the arm.

In order to determine the *duration of immunity* from vaccination, W. P. Dearing and M. J. Rosenau (J. A. M. A. 102:1998 (June 16) 1934) investigated the records of 557 medical students who had been vaccinated previously. In summarizing the results, they found that revaccination of a group of 337 students who had successful primary "takes" less than 10 years before, produced only 1 primary take; the revaccination of 168 students who had had "takes" 10 to 19 years before, gave 6 primary reactions, or 4 per cent. of the group; of 52 vaccinated more than 20 years before, 4 or 8 per cent. had primary takes. The remainder of each group had immediate or accelerated reactions. There were 9 other students who had a history of smallpox infections but had never been vaccinated. Four of this group developed primary takes. The authors concluded that the vaccination with cowpox offered a better protection against smallpox than an attack of the disease itself, and this protection seemed to last 20 years or more in most individuals rather than the traditional 7 to 10 years.

With carefully standardized technic, R. F. Parker and R. S. Muckenfuss (J. Infect. Dis. 53:44 (July-Aug.) 1933) were able to demonstrate a specific complement fixation reaction between vaccinia virus and its immune serum. The potency of the serum and the time allowed for the reaction were important factors and the removal of the virus from the antigen did not effect the reaction. Employing fluid from smallpox vesicles as an antigen, specific complement fixation was obtained with antivaccinal rabbit serum, while other antigens from chickenpox or other skin lesions did not produce false positive results. Material collected from vaccinia or smallpox lesions within 13 days after the appearance of the eruption gave positive tests and this was thought to be of assistance in making an early diagnosis of the disease.

*Complications of Vaccination*—Meningitis occurring as a sequela of smallpox vaccination was described by F. Wernick (Deutsche med. Wchnschr. 15:1434 (Sept. 15) 1933). Six days after inoculation with vaccine virus, the child developed diminished pupillary and corneal reflexes, an absence of the patellar reflexes, and loss of sensation of the skin. Convulsions, a weak, rapid pulse, restlessness and coma followed quickly and the patient died the next day. At autopsy there was early inflammation of the meninges.

An instance of *postvaccinal encephalitis* in a child 5 years of age was reported by S. Newman (J. Pediat. 3:461 (Sept.) 1933). Two days after vaccination, this child complained of pain in the stomach and head, followed quickly by vomiting and progressive drowsiness. On the fourteenth day after vaccination, he was somnolent, had a slightly positive Kernig sign bilaterally, a rigid neck, hyperesthesia of the skin, internal strabismus, and a ptosis of the right upper eyelid.

The cerebrospinal fluid was under increased pressure and contained 15 to 20 lymphocytes and an increased amount of globulin. Within the next 12 days the patient improved except for the ptosis of his eyelids, which did not disappear until several months later. In a review of the literature it was found that this was the seventy-fifth case of postvaccinal encephalitis to be reported in the United States during the last 10 years.

In 2 infants with encephalitic complications following vaccination, V. Ochsenius (Monatschr. f. Kinderh. 58:207 (July) 1933) noticed that the "takes" were unusually extensive and the local reactions severe. He believed that the methods of inoculation frequently introduce the lymph over too large an area and too deep into the skin tissues, leading to the severe takes which may be responsible for complications of the central nervous system.

The *activation of old tuberculous lesions* followed smallpox vaccination in 4 patients observed by W. Blacher (Jahrb. f. Kinderh. 142:26 (Feb.) 1934). Although it was difficult to prove that the vaccination was the cause of the exacerbation of these infections, the sequence of events was sufficient to arouse suspicion. The writer concluded that in certain patients who are not in the best physical condition or are suffering from some illness, the vaccination should be postponed or done in a way which would produce a small, mild "take."

The lesions of *vaccinia* were observed from a histologic and experimental viewpoint by J. H. Dible and H. H. Gleave (J. Path. and Bact. 38:29 (Jan.) 1934). True vaccinia is characterized by a generalized eruption and infection due to the dissemination of the vaccine virus by the blood stream. A typical patient described by the authors was a boy, 3 months of age, who developed a generalized eruption of vesicles and pustules on the wrists, thighs, legs and head, 19 days after vaccination. At the site of the original "take" on the arm was a large red area surrounded with vesicles which was first noticed on the sixteenth day. The child had severe systemic symptoms and died 4 days later. In order to determine whether this virus of vaccinia had become so modified that it resembled human variola, some of the vesicular fluid from the patient's lesions was inoculated on the skin of rabbits. The "takes" observed there indicated that the virus had retained its vaccine characteristics. Any variolous transformation of this virus would not have produced "takes" on the rabbit.

A method recently employed to reduce the severity of the *local reaction* of a vaccination by treatment with **x-rays** was described by E. Barla-Szabó (Arch. f. Kinderh. 101:1 (Dec.) 1933). On the eighth day after the inoculation of vaccine virus on both arms of a patient, one of the arms was treated with x-ray exposure. Within 2 to 5 days the hyperemia and the infiltration were considerably diminished in comparison with the reaction on the control arm. A group of 37 patients was treated with a single dose of the x-ray therapy and those who had severe local reactions received a second treatment 2 days later. The results were very satisfactory. The hastened recovery from the vaccination reaction did not seem to impair the degree of immunity derived from the vaccine virus.

The *virulence* of vaccine lymph is greatly *reduced* also by *exposure to daylight* or to *direct sun rays*. N. M. Goschanskaja and D. S. Stachastny (Zentralbl. f. Bakt. (Abt. 1) 129:50 (July 11) 1933) exposed a quantity of vaccine lymph

20 mm thick to diffuse daylight at an average temperature of 21° to 24° C. and the lymph lost its virulence after a period of 10 days. When the column of lymph was 9 mm. in thickness, that of the ordinary ampoule in his locality, the potency was diminished in 5 to 7 days. Direct sun rays reduced the virulence of vaccine material of high potency in 2 to 3 hours and that of less virulence in an hour. Light rather than heat was the factor which caused a decrease in the potency, and the weaker the lymph and the thinner the layer, the more rapid was the destructive effect of the light.

**SYPHILIS, CONGENITAL.—Incidence.**—In France the incidence of the disease varies from 2 per cent, as reported by Nassau, to 25 per cent., reported by Marfan.

At the Cook County Hospital among 101 newborn infants with a four-plus Wassermann reaction, A. H. Parmelee (Illinois M. J. 64. 131 (Aug) 1933) found that 26 per cent had suggestive clinical symptoms; 13.7 per cent. had positive Wassermann and Kahn tests; while 54 per cent had bone changes sufficiently marked to warrant a diagnosis of congenital syphilis. On these findings the author emphasizes the importance of x-ray examination of the bones because in congenital syphilis the x-ray may show the presence of an osteochondritis or periostitis in patients without clinical or serologic evidence of the disease.

F. Terrien (Bruxelles-méd 14. 333 (Jan 7) 1934) reports the age incidence of interstitial keratitis among 510 cases at the Hotel Dieu, in Paris. Among these 12 per cent were under 5 years, 50 per cent between 5 and 15, 30 per cent between 16 and 25, and 8 per cent over 25 years. Two-thirds of the cases were in girls. This writer emphasizes the importance of the slit lamp examination in the early diagnosis of interstitial keratitis.

F. R. Smith (Bull Johns Hopkins Hosp 53. 231 (July) 1933) reported finding an incidence of 50 per cent white patients in a group of 462 late heredo-syphilitics, 59 per cent of these were females as contrasted to 34 per cent. white and 49 per cent female in an adult syphilitic group. The active lesions fell into 5 major groups: ocular, which was overwhelmingly interstitial keratitis; osseous, including periostitis or osteitis of the long or flat bones, arthritis, and synovitis; nerve deafness, neurosyphilis and a small group, composed of gummatous lesions of the skin, mucosæ, or viscera. Ocular lesions and nerve deafness occurred with equal frequency in both colored and white races and in both sexes. Osseous lesions were more than twice as common in white patients as in negroes, an exact reversal of the racial distribution in the acquired disease. Neurosyphilis is much more frequent in whites than in negroes, and the sexes were equally affected in this series, while in acquired syphilis there is higher incidence in males than in females. Nerve deafness usually occurred in the absence of other clinical or serological evidence of neurosyphilis.

Of 402 mentally defective children, mostly low grade, K. C. L. Paddle (Brit J Child Dis. 30. 249 (Oct-Dec) 1933) found 37 cases to be of hereditary syphilis, or an incidence of 9.2 per cent. In the group of congenital syphilitics, 12 had abnormal cerebrospinal fluids and of these 5 gave strong paretic curves, but none of these cases could on clinical grounds be regarded as juvenile general

paralysis. On the other hand, the cerebrospinal fluid of 29 mongols failed to give any type of curve with the colloidal gold reaction. In 60 per cent. of the congenital syphilitic defectives there was a marked retardation in the descent of the testes.

**Relationship of Other Diseases.**—N. J. Spyropoulos and G. Georgaras (Arch. de med. d. enf. 37:97 (Feb.) 1934) report a case of *Raynaud's syndrome* in a young 2½-year-old syphilitic infant. The authors pointed out the relation of another factor, *cold and dampness*, to the vascular disorder. The child's Wassermann was strongly positive in this case. All the symptoms disappeared under antisyphilitic therapy. R. Dupérié (*Ibid.* 36.425, 1933) described his observations on the relationship of the *hypophysis* to hereditary syphilis. He believes that on the basis of the pathological changes found in the gland many of the dystrophies of congenital syphilis can be explained. M. Péhu, and J. Bouctomont (Rev. franç. de pédiat. 9.664, 1933) report a case of congenital syphilis causing *Pott's disease* in a child 15 months old. Their findings were checked by x-ray and anatomic studies. In the cartilages of the bodies of the vertebræ was found tissue which was diagnosed as an intertrabecular gumma. Other evidence of osseous syphilis in this child included hyperostoses of the anterior border of the lumbar vertebræ and gumma of the femur with syphilitic periostitis. The authors believe that certain mechanical conditions, such as weight bearing, may have modified the circulation of that region and contributed to the alterations in the cartilage. A case of *pes cavus* in a congenitally syphilitic 13-year-old child is reported by C. W. Goff (Am. J. Surg. 22.359 (Nov.) 1933) who found on further examination a four-plus Wassermann and Kahn reaction, with a spinal fluid showing a typical juvenile tabetic gold curve. Antiluetic treatment produced a diminution of spasticity of the legs and feet, and greater ability of the child to stand erectly. W. Mikulowski (Rev. franc. de Pédiat. 9.767, 1933) believes that congenital syphilis is able to provoke *diabetes*. Up to 1929, the percentage of diabetes in his group of congenital syphilitics at the Charles and Marie Hospital at Varsovie was 45 per cent. Since then it has risen to 71.4 per cent.

Orman Perkins (Am. J. Dis. Child. 46.1432 (Dec.) 1933) reports the cases of 4 children as representing a type of familial, diffuse *sclerosis of the brain*, a disease which has become a part of the chromosome pattern in this family, producing a type that is abnormal and degenerate. He believes that the responsible factor in the production of this rare and interesting degenerative process is syphilis and it is his opinion that this condition should be included in the endogenous familial forms described by M. Bielschowsky and R. Henneberg (J. f. Psychol. u. Neurol. 36.131 (May) 1928), and known as *Merzbacher-Pelizaeus disease* or *aplusia axialis extracorticalis congenita*.

**Diagnosis.**—In studying the *cerebrospinal fluid* of 30 newborn infants born of luetic mothers, M. Gleich (Arch. Pediat. 50.457 (July) 1933) found that the Kahn test was negative in every case. This paralleled the blood Kahn and Wassermann tests in the same infants. The blood and spinal fluid Kahn test are usually negative in the first 2 weeks of life in infants with congenital lues. No clinical signs may appear during this time. In the third or fourth week the blood and

spinal fluid Kahn are frequently positive, coincident with the appearance of a macular rash, condylomata, snuffles, periostitis, a hard small palpable spleen and small shotty epitrochlear glands. The Lange-colloidal gold test was of no value. Several of the control cases showed a luetic reaction or meningeal irritation.

W. Mikulowski (Ann. de dermat. et syph. 4:861 (Sept.) 1933) advises examining the *hands* in studying the stigmata of congenital syphilis. A number of stigmata of the hands have been described, including the characteristic syndactylism of syphilis, brachydactylism, polydactylism, Bouchard's nodules between the first 2 phalanges, exaggerated flexibility of the fingers, violet circles on the nails, and shortening of the little finger or thumb. The author describes a new stigma consisting of *asymmetry of the fingers* found in 80 per cent of his cases of congenital syphilis. There may be a difference of as much as 3 cm. in the length of the corresponding fingers of the two hands. J Cathala (Paris méd 2:329 (Oct) 1933) calls attention to the *osteochondritis* of Wegner in the newborn, the *habitual vomiting* of Marfan, and the *isolated convulsions* described by Marfan. In older children, all *obscure anemias* or *dystrophies* should arouse suspicion. Treatment should be given in all cases of doubt.

SERODIAGNOSIS.—According to L. Chargin and M. Umansky (Am. J. Syph. 17:468 (Oct) 1933), it is an established fact that the Wassermann test may be negative at birth and first become positive many months later, as long as a year or more, but it cannot be readily explained. Even assuming that the infant became infected during the very last days of the intrauterine life or while being born, it would be expected that the Wassermann test would become positive not later than 3 months postpartum; yet this is not always the case. In congenital syphilis, as in the acquired form of the disease, the disappearance of clinical manifestations under antisyphilitic treatment is usually prompt even under mild therapy, and clinical symptoms cannot be taken as a guide to the efficacy of therapy. On the other hand, it is well known that the Wassermann test persists long beyond the disappearance of clinical signs and is a difficult symptom to influence. Experience has taught that in the untreated congenitally syphilitic child, the Wassermann test is one of the most persistent of symptoms. Although clinical manifestations of the disease disappear frequently without antisyphilitic therapy, this is not the case, or rarely so, with the Wassermann test. Consequently, the Wassermann test forms an excellent guide in judging the effect of treatment.

In 115 out of 402 patients in whom Wassermann reversal was accomplished by treatment, F. R. Smith (*loc cit*) found that there was subsequently serologic relapse in 27, leaving only 79 patients of the total number with permanent serologic reversal. As to the relationship of Wassermann fastness to ultimate clinical outcome in late congenital syphilis, it appears that a satisfactory clinical outcome with freedom from progression or relapse is obtained with equal frequency whether or not the Wassermann becomes negative. In other words, Wassermann fastness in late congenital syphilis is not of unfavorable prognostic import for the patient's future course. In late congenital as in late acquired syphilis, persistent Wassermann positivity, during and after treatment, is much more likely to be an

expression of the delicacy of the serologic test than an index of clinical or pathologic activity of the disease

**Prognosis.**—F. R. Smith (*loc cit.*) studied 462 patients over 13 years of age to determine the results of treatment in the late form of the disease. He suggests that in the late congenital, as in the acquired infection, symptomatic neurosyphilis indicates the probability of the development of clinical neurosyphilis, while a normal spinal fluid is a practical guarantee against such a disaster. Further, that the congenital syphilitic is more likely to develop some lesion at some time than the adult with the acquired infection; neither race nor sex confers protection against any type of lesion except those involving the nervous system or the bones. Aside from deaths due to juvenile paresis, there were no deaths attributable to syphilis. It seems clear that late congenital syphilis rarely, if ever, causes death in the absence of involvement of the central nervous system. In cases of interstitial keratitis improvement occurs only in those patients with acute lesions; scars are irremediable or nearly so. When the acute interstitial keratitis was unilateral, it usually remained so.

**Prophylaxis.**—It is commonly agreed upon that the most effective prophylactic remedy is the recognition and treatment of the disease in the pregnant mother. F. Terrien (*loc cit.*) states that the only effective way to combat the disease is **prophylactic treatment of the mothers** which, if thoroughly and systematically carried out, would practically eradicate congenital syphilis and all its manifestations. Care should be exercised in the choice of donors for blood transfusions as shown by G. R. Williamson and R. A. Strong (*Am J Syph* 17:484 (Oct) 1933) who report a case of transmission of congenital syphilis to an unborn baby as a result of a transfusion to its mother during pregnancy from a presumably syphilitic donor.

**Treatment.**—Among the arsenicals, a drug that is gaining in favor in this country is **acetarsone**, known as **stovarsol** in France and as **spirocid** in Germany. The drug is odorless, soluble in water, and is marketed in 0.1 Gm. and 0.25 Gm. ( $1\frac{1}{2}$  and 4 grains) tablets. According to A. S. Traisman (*Am J Dis Child* 46:1027 (Nov pt 1) 1933), it contains between 27.1 and 27.4 per cent arsenic as compared to 19 per cent in neoarsphenamine and 21 per cent in sulpharsphenamine. The dosage varies widely as to the total quantity to be administered and the duration of the course of treatment. The great variety of dosages used emphasizes the fact that no hard and fast rule can be employed as yet. The tolerance of the patient must be considered and the possibility of hypersensitiveness to the drug taken into account. The treatment should be started in doses which are considerably below the optimal dose and then gradually increased.

The *dosage* advocated by Bratusch-Marrain was used by H. A. Rosenbaum (*J Pediat* 3:434 (Sept) 1933) in his survey of 100 cases treated with this drug. The plan is as follows: 0.005 Gm. ( $\frac{1}{20}$  grain) of acetarsone per kg. ( $2\frac{1}{5}$  lbs.) body weight for 1 week followed by 0.010 Gm. ( $\frac{1}{10}$  grain) per kg. daily for 1 week, 0.015 Gm. ( $\frac{1}{4}$  grain) per kg. daily for 1 week, and 0.020 Gm. ( $\frac{1}{5}$  grain) per kg. daily for 6 weeks. Rest for 1 month. The course is repeated until the serologic tests are negative. Three courses are then given, followed by a rest period of 6 months and one more course. Method of administration. For

small infants the mother is advised to crush the amount of acetarsone ordered, to dissolve it in water and to give it  $\frac{1}{2}$  hour before feeding time. When the dose ordered was large, as for the older child, the instructions were that the medication be divided equally in 2 or 3 doses and that it be given in water 1 hour before meals. Traisman (*loc. cit.*) advises giving only enough acetarsone for 1 week, with instructions as to the amount to be given at each feeding and how to administer it. The parent is warned that at the first sign of fever, diarrhea, vomiting, or the appearance of a rash, the medication should be discontinued at once and the child returned to the clinic. The parent is also warned to keep the drug out of reach of the children in the family. Each patient in his group returned to the clinic weekly for physical examination, for urinalysis, and for the weekly supply of acetarsone. In this manner each child was kept under close observation during the whole course of treatment. *Toxic symptoms* from the drug occur occasionally, but they are usually mild. A. C. Rembar (*J. Pediat.* 3:841 (Dec.) 1933) noted 3 cases of diarrhea in 32 premature infants. In each case this occurred during the fifth or sixth week of treatment, after a total dosage of from 2.5 to 3 Gm (38 to 45 grains) of the drug. F. Eckardt (*Jahrb. f. Kinderh.* 141:278, 1934) used acetarsone in the treatment of children with proved syphilis, using 12 to 15 Gm (3 to  $3\frac{3}{4}$  drams) of the drug in a 12-week period. Visible evidences of improvement are manifested by a surprising improvement in the general condition of the patient, frequently a gain in weight and disappearance of skin lesions. He felt that the more severe forms of visceral syphilis are not influenced by acetarsone more than by other forms of treatment. Traisman (*loc. cit.*) reports that all the osseous changes were completely healed after one course of treatment, and that all his patients in their study showed consistent weight gains. Most writers agree that the chief advantage of acetarsone lies in its ease of administration, and the resulting cooperation of the parents.

**Bismuth** in various forms has been used by A. N. Accinelli, R. N. A. Janzon and M. Seoane (*Semana med.* 1:2052 (June 22) 1933), who treated 38 children with soluble and insoluble preparations. The insoluble preparation, **iodo-bismuthate of quinine**, was given in doses of 0.002 mg per kg of weight, an injection being given every 4 days. The total dose was 0.024 mg per kg. of weight given in 12 injections. The liposoluble preparation was given in doses of 0.001 mg per kg of weight, one injection being given every 4 days. The total dose was 0.012 mg kg of weight given in 12 injections. The liposoluble bismuth proved superior to the insoluble form in their study. In an effort to prevent congenital syphilis in the child, S. J. Zakon (*Urol and Cutan Rev.* 38:250 (April) 1934) used minimal doses of **bismuth salicylate** in oil in 0.13 Gm doses (2 cc) injected intramuscularly once a week throughout the entire period of pregnancy. C. S. Wright (*Pennsylvania M. J.* 36:832 (Aug.) 1933) studied a group of 75 children of whom 27 were given **bismuth** alone, and 48 arsenicals and bismuth. The serologic results were better in the first group. S. Irgang (*Arch. Pediat.* 50:477 (July) 1933) believes that bismuth is relatively nontoxic, that bismuth and mercury should not be given together in the same course of treatment and that bismuth should be given only by the intramuscular route. The author prefers the insoluble compounds, as a 10 per cent. suspension

of bismuth salicylate in a vegetable oil. Bismuth in the form of bismuth salicylate, 1 c c. (16 minims) of suspension, is equivalent to 50 mg. ( $\frac{5}{8}$  grain) of metallic bismuth.

Dosage table of bismuth salicylate is as follows :

1st 4 weeks . . . . .	0.25 c c (4 minims) or 12.5 mg. ( $\frac{1}{8}$ grain) of metallic bismuth.
1 to 3 months ..	0.25 to 0.50 c c (4 to 8 minims) of suspension.
3 to 12 months .	0.5 c c (8 minims) of suspension.
1 to 4 years ...	0.75 c c (12 minims) of suspension.
4 to 7 years .	0.75 c c to 1.0 c c (12 to 16 minims) of suspension
8 yrs. and above	1.0 c c. (16 minims) of suspension.

These injections should be given intramuscularly once weekly for 12 to 15 weeks. If a soluble bismuth preparation is used, the weekly dose should be less than that given above. The total weekly dose of a soluble compound is not injected at one time; one-half of the specified dose is injected twice weekly. This prevents too rapid absorption of large doses of the drug.

**TUBERCULOSIS IN CHILDREN.**—*Diagnosis.*—The establishment of a certified diagnosis of *pulmonary tuberculosis* in children is frequently difficult and the clinical diagnosis must of necessity be made by the method of elimination. In recent years more and more dependence is being placed upon interpretations of the x-ray pictures, particularly in connection with the use of the tuberculin test. The difficulty in the evaluation and interpretation of abnormal shadows in the x-ray films of children is well known. The x-ray appearance of chests of children with chronic respiratory infections and negative tuberculin skin tests is frequently quite similar to those of children with positive tests. In an attempt to determine more accurately the x-ray appearance of tuberculous chest pathology, M. L. Bronson, H. M. Zimmerman and G. F. Powers (Am J Dis Child 47: 104 (Jan.) 1934) have made an attempt to correlate the x-ray appearance of the chest with the clinical and pathologic findings in 14 tuberculous children. While this material is not extensive, the study is thorough and might well be extended by other investigators.

On the basis of their experience, they make the following recommendations for x-ray technique: (1) Exposure should be made with the chest in full inspiration and (2) at 6-foot target-film distance, (3) oblique views of the chest are valuable for the detection of mediastinal pathology, (4) in order to bring out calcium deposits clearly, films should not be underexposed (soft), (5) serial x-ray pictures should be taken during the course of the disease.

The following observations are extracted from the "general comment" in this article.

Large homogeneous lobar shadows, mottled shadows (disseminated or localized) or so-called "infiltration" may or may not be caused by tuberculosis, the interpretation of these shadows is often unduly influenced by a knowledge of the age of the patient and his reaction to tuberculin.

Calcium deposits in the parenchymal lymph nodes or pleura are indicative of a tuberculous process in a vast majority of instances. "Oblique roentgenograms" may show calcium deposits in the mediastinum which are obscured on the usual anteroposterior exposure.



The x-ray demonstration of cavity formation is of equal importance with the presence of calcium as a diagnostic sign. However, caseous débris within the cavity may prohibit its detection both clinically and radiologically. On the other hand, the x-ray pictures may suggest cavities when there are none.

The x-ray appearance of chronic nontuberculous bronchopneumonia with bronchiectasis may be quite similar to that of tuberculous ulcerative bronchitis with adjacent consolidated pulmonary tissue. The apparently dilated bronchi may be seen at times within the shadow and cavities are also frequently present in the tuberculous lesion. As a general rule, the shadows produced by the nontuberculous bronchopneumonia with bronchiectasis do not have the smooth, homogeneous appearance (except for the bronchial markings) of the tuberculous consolidation. This is as would be expected, since the tuberculous process is a diffuse parenchymatous one, whereas the nontuberculous pneumonia under discussion is a focal, peribronchial lesion.

It is also pointed out that there may be little or no evidence of pulmonary pathology on the x-ray film when the lungs are the seat of extensive and proved pathologic processes.

Generalized so-called miliary shadows or snow-flake infiltration, which is generally regarded as pathognomonic of generalized tuberculosis, may be closely simulated by certain forms of nontuberculous pneumonia. If there are no evidences of calcium deposits and the miliary shadows are not sharply circumscribed, the only important differential point which the authors have found is concerned with the peripheral fields of the lungs. If there are disseminated areas of consolidation here, the miliary lesions are more apt to be tuberculous than if the peripheries are clear.

Despite the constancy of associated involvement of the tracheobronchial lymph nodes with primary pulmonary tuberculosis, the actual demonstration of tuberculous lymphadenitis by the x-rays is not always possible. From a technical standpoint, close target-film distance, rotation of the chest and the expiratory phase of respiration may account for changes in the contour and size of the mediastinal shadow incorrectly suggestive of large lymph nodes. Calcium shadows in the mediastinal and hilar regions are usually tuberculous in origin. The lymph node itself may not be visualized on the x-ray picture unless it protrudes beyond the usual cardiac, vertebral or mediastinal shadows. When, under proper technical conditions, a bulging hilar or mediastinal shadow of homogeneous density and well demarcated outline consistently appears on the x-ray picture taken from time to time of a child with a positive reaction to tuberculin, a diagnosis of tuberculous tracheobronchial nodes is warranted if there is no other explanation of the shadow. However, only the presence of calcium in these shadows makes a purely x-ray diagnosis of tuberculous lymphadenitis highly probable.

With the increased use of the tuberculin test and of x-ray examinations there has been some tendency to minimize the value of the history and physical examination in the diagnosis of pulmonary tuberculosis in children. It is quite true that a child with active pulmonary disease may have no symptoms or none of those commonly associated with pulmonary tuberculosis and there may be no

known history of contact. Further, it may be impossible to detect by physical examination pulmonary disease which is shown by the x-rays. These facts are stated not to detract further from the value of the history and physical examination, for the clinician should rather be more alert in their use. However, it seems quite plain, in view of the changing conception of tuberculous disease as a family or group infection rather than of only the individual patient, that the tuberculin test and the x-rays should be used for the detection of tuberculous disease in the members of the family or group of the diagnosed patient. In a general article on the diagnosis and prognosis of tuberculosis in children A. G. Mitchell and W. E. Nelson (*Ohio State M. J.* 30:357 (June) 1934) cite an instance which emphasizes the importance of this statement. The roentgeno-

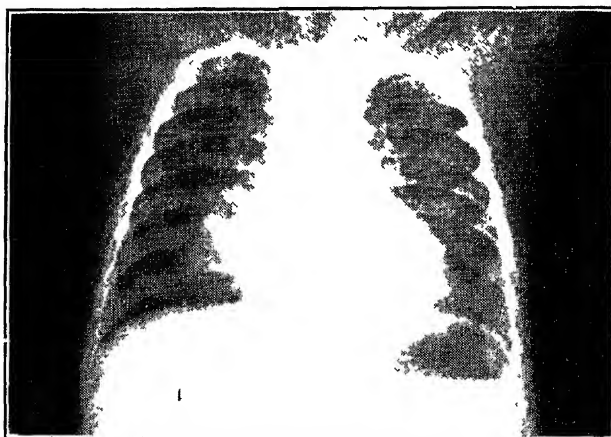


Fig 1—Roentgenogram taken 7-29-'32 Shows exudative lesion in right hilus region extending into right base (Mitchell and Nelson *Ohio State M J*)

gram of an 8-months-old colored infant revealed an exudative lesion in the right hilar region extending into the right base (Fig 1) The tuberculin reaction was positive The mother knew of no possible contact with tuberculous infection Roentgenograms of the mother's chest showed a left basal lesion (Fig 2) Tubercle bacilli were found in her sputum



Fig 2—Roentgenogram of mother, aged 19 years, taken 6-11-'32 Shows basal lesion of left side. Sputum positive (Mitchell and Nelson *Ohio State M J*)

*Miliary Tuberculosis.*—Occasionally x-ray pictures are taken postmortem in an attempt to establish an otherwise obscure diagnosis, particularly when a necropsy is not permitted. W. E. Anspach (Am. J. Roentgenol 30:768 (Dec.) 1933) has shown that minute hemorrhages within the lung which apparently occur as death takes place may cast shadows on the x-ray film which appear quite like those of miliary tuberculosis. An instance of larger pulmonary hemorrhages as well as one of minute petechial hemorrhages is reported. In the case of larger hemorrhages, the x-ray pictures may simulate other pulmonary lesions. Thus, a mistaken interpretation could easily be made if the necropsy x-ray picture is relied upon for diagnostic purposes.

*Bacilli in Gastric Contents*—Further reports of the isolation of tubercle bacilli from gastric contents and feces of infants and children are found in the literature of the past year. Among them are papers by I. Gourley (Am. Rev. Tuberc 29:461 (Apr.) 1934), L. Mishulow, C. Kereszturi and D. Hauptman (*Ibid.* 471), J. P. Nalbant (*Ibid.* 481), V. Poulsen and A. D. Anderson (Am. J. Dis. Child. 47:307 (Feb.) 1934) and V. Lester (*Ibid.* 322). It is presumed that tubercle bacilli get into the stomach from swallowed pulmonary exudate. Hence, the reasons for the search for tubercle bacilli in the stomach contents of children are essentially the same as those for the examination of sputum of adults. Of particular interest and importance are the reported findings of tubercle bacilli in the lavaged stomach contents of children without demonstrable pulmonary involvement, some of whom are apparently well children whose only other evidence of tuberculosis is a positive tuberculin reaction. What this means in terms of active infection for the child himself and whether or not he is a source of infection for others are two important questions which to date have not been satisfactorily answered. The x-rays have come to be considered the most sensitive and accurate means for determination of pulmonary lesions, and serial pictures are the best available index of the progression of the lesion. Yet tubercle bacilli have been found in the stomach contents both of children whose x-ray pictures of the chest do not reveal pulmonary pathology, as well as in the lavaged material from children whose pictures show evidence of apparent healing as evidenced by calcification.

According to Poulsen and Anderson (*loc cit*), the younger the child with a positive tuberculin reaction, the more likely is he to discharge tubercle bacilli, since the tuberculous process has had less time to heal. Thus, in their examination of 622 children with positive tuberculin reactions, 160 of 383 children under 4 years of age had tubercle bacilli in their lavaged gastric contents, whereas bacilli were found in the stomach contents of only 39 of 239 children from 4 to 10 years of age. There was no x-ray evidence of pulmonary pathology in 31 of the 199 children showing tubercle bacilli in lavage.

In regard to *prognosis*, follow up studies of these children did not reveal any significant differences between those who did and those who did not have tubercle bacilli in their stomach contents.

V. Lester (*loc cit*) found no evidence to indicate that the bacteria obtained by gastric lavage were less virulent than tubercle bacilli isolated from other parts of the human body. In view of certain objections to and difficulties in securing

gastric contents for analysis, it is interesting to note that Mishulow and her coworkers feel that repeated examination of feces may prove to be as satisfactory a method as the examination of gastric contents.

*Bacillema*.—In the hands of K. Rupilius (Arch. f. Kinderh. 101: 48 (Dec.) 1933) the search for tubercle bacilli in the blood of children by the Lowenstein method is not as apt to be as successful as the examination of gastric contents, feces, urine and material from draining sinuses. In only 3 of 96 children suspected of having tuberculosis was he able to isolate tubercle bacilli from the blood stream. It is interesting to note that 2 of the 3 children had rheumatic arthritis. Both had positive tuberculin reactions. Rupilius definitely states that no significance should be attached to reports of tuberculous bacillemas in children with rheumatic arthritis and chorea who have negative tuberculin reactions.

*Tuberculin*.—During the past year a new tuberculin skin testing material, "P. P. D." (Purified Protein Derivative) which is sponsored by the Committee on Medical Research of the National Tuberculosis Association, has been placed on the market. Reference to this product has already been made in the original article "Tuberculosis in Infancy and Childhood" (CYCLOPEDIA OF MEDICINE, Vol. XII, p. 387).

Using filtrates of tuberculous ultravirus, J. Valtis, G. Paiseau and F. van Deirse (Ann. Inst. Pasteur 51: 584 (Nov.) 1933) have elicited skin reactions in newborns from tuberculous mothers when the infant failed to react to tuberculin even in high concentration. This they take as one more evidence of the transplacental transmission of ultravirus of the tubercle bacillus. They further believe that the use of the ultravirus filtrate may be an added aid in diagnosing tuberculosis when no reaction is obtained from the use of tuberculin.

*Complications*.—*Pneumothorax* is not a frequent complication of pulmonary tuberculosis in children and is rare in infants. To the collected cases of tuberculous pneumothorax in infants under 2 years of age, 2 are added by J. Greengard and I. R. Abrams (Am. Rev. Tuberc. 28: 236 (Aug.) 1933). They suggest that the relative infrequency of such a complication may be due to the fact that rapidly progressive primary tuberculous lesions are apt to invade the blood stream and terminate in a generalized infection. The chief difference between tuberculous pneumothorax in infancy and that in adults is the lack of sudden onset with severe pain and symptoms of circulatory collapse in infants. In neither of the authors' patients was the presence of air in the pleural space suspected before the physical and x-ray examinations were made. Both of these patients died and the authors believe that the presence of a tuberculous pneumothorax is indicative of a grave prognosis.

*Erythema Nodosum*.—Further evidence to support the contention that erythema nodosum occurs early in the course of a primary tuberculous infection and marks the beginning of the period of allergy is submitted by E. Gamstedt (Monatschr. f. Kinderh. 59: 111, 1933). Seventy-five tuberculin tests were performed on 51 children who later developed erythema nodosum. All of the tests were negative in spite of large doses of tuberculin. In one instance there was a negative Mantoux reaction to 3 mg. of tuberculin, 4 days before the onset of the fever of erythema nodosum. The tuberculin reactions were positive

in all but one case after the onset of the fever and eruption. In this instance the Pirquet test was negative 2 days after the onset of fever but was positive 5 days later.

H. Ernberg (Am. J. Dis. Child. 46:1297 (Dec.) 1933) also believes that erythema nodosum is an evidence of tuberculous infection and may be regarded as an autogenous tuberculin reaction. The erythema nodosum appears early in the course of the tuberculous infection and marks the transition from the pre-allergic to the allergic stage. In certain instances, however, erythema nodosum may follow an alteration of the allergic state following an acute infectious disease or other condition.

*Phlyctenular Conjunctivitis*—Further evidence to support the contention that there is an etiologic relationship between tuberculosis and phlyctenular conjunctivitis is given by M. Goldstein and C. L. Wood (*Ibid.* 47:171 (Jan.) 1934). In a group of 71 children from 10 months to 12 years of age with phlyctenulosis, they found x-ray evidence of tuberculosis in 48, suggestive evidence in 13, and the films were interpreted as negative in only 10 instances. Tuberculin tests were positive in 58 of 60 children tested. No condition other than tuberculosis was found in a proportion large enough to indicate an etiologic rôle. It is of interest to note that in 18 instances the only x-ray evidence of tuberculosis was found in the neck and abdomen. They conclude that although it may be possible that there is a relatively uncommon form of conjunctivitis clinically difficult at the onset to distinguish from tuberculous phlyctenulosis, which is caused by some other factor, in the vast majority of cases of phlyctenular conjunctivitis careful study will reveal the presence of underlying tuberculous infection.

*Immunity*.—In the 1934 SUPPLEMENT reference was made to F. B. Seibert's (J. Infect. Dis. 51:383 (Nov.-Dec.) 1932) demonstration of induced tuberculin sensitivity in nontuberculous animals by means of injection of tuberculo-protein. This has been confirmed by K. C. Smithburn, F. R. Sabin and J. T. Geiger (Am. Rev. Tuberc. 29:562 (May) 1934) who used M.A-100 tuberculo-protein for both the sensitizing and testing media. Rabbits and guinea-pigs so sensitized were then injected with virulent tubercle bacilli. Nontuberculin sensitized and nontuberculous animals were also injected with tubercle bacilli as controls. The previous injection of tuberculo-protein had no demonstrable effect upon the resistance of the animals to tuberculous infection. The authors interpret this observation as another link in the chain of evidence which tends to dissociate allergy from immunity.

Further data of a different type which tend to show that the allergic and immune phenomena are separate factors have been collected by J. A. Johnston, P. J. Howard and J. Maroney (*Ibid.* 29:652 (June) 1934). The reaction to tuberculin was studied in a group of children throughout the period of the primary complex, roughly about 2 years. Tuberculin tests were made at monthly intervals and serial x-ray pictures of the chest were made. It was found that the reaction to tuberculin during the evolution of the primary complex followed a curve which rose to a high peak after the absorption of the parenchymal lesion and which corresponded with the maximal involvement of

the hilar lymph nodes. The intensity of the reaction declined with the diminution in size of the nodes and their calcification. While this course of events was usually paralleled by peripheral blood changes associated with healing, the same tuberculin course was seen when the x-ray picture showed absorption but the blood picture remained equivocal, or even showed retrogression.

**Prognosis.**—Articles reporting recovery from pulmonary tuberculosis in infancy and early childhood are becoming more frequent. Among these are reports by L G Parsons (*Lancet* 1:1101 (May 26) 1934), A G Mitchell and W. E. Nelson (*loc cit*), H S. Reichle (*Am J. Dis Child.* 46:969 (Nov) 1933) and E C. Dunham (*Ibid.* 47:149 (Jan) 1934). Figs. 3, 4 and 5 taken from the article by Mitchell and Nelson illustrate an example of retrogression



Fig. 3—Roentgenogram taken at time of hospital admission. Shows consolidative lesions of left upper lobe and diffuse lesions of right upper lobe (Mitchell and Nelson (*Ohio State M J*))

of extensive infiltrative pulmonary lesions in a 7-months-old colored infant. It is in order to note here that both Parsons and Reichle (See also 1934 SUPPLEMENT, p 936) question the designation of such consolidative lesions as the one in the left upper lobe of this case as epituberculosis or nonspecific infiltration and believe them to be actual tuberculous involvement which undergoes resolution. It may be observed that in this instance healing is followed by distinct calcification in this area. This is not supposed to follow the supposedly allergic reaction of so-called epituberculosis.

J A Myers (*Am Rev Tuberc* 28:793 (Dec) 1933) continues to maintain that the initial infection with the tubercle bacillus is invariably a benign one and that the danger lies in the preparation of the tissues for the reinfection or adult type of tuberculosis. It is needless to say that there are many who continue to believe that there is evidence to support the contention that the initial infection confers at least partial immunity.

**Sedimentation Rate.**—W. A. Reilly (*Ibid* 29:220 (Feb) 1934) has observed the blood sedimentation rate over a 6-month period in a group of 36 tuberculous

girls. He confirms the opinion of those other investigators who believe it to be a fairly reliable index for gauging activity and prognosis. It has little or no value other than presumptive in diagnosis. Repeated tests in the individual patient may show the trend of the infection when the temperature, weight and white cell count do not. The author believes that the sedimentation rate is secondary only to the x-rays as a means of determining progress and particularly that it is more sensitive than the monocytic-lymphocytic ratio.

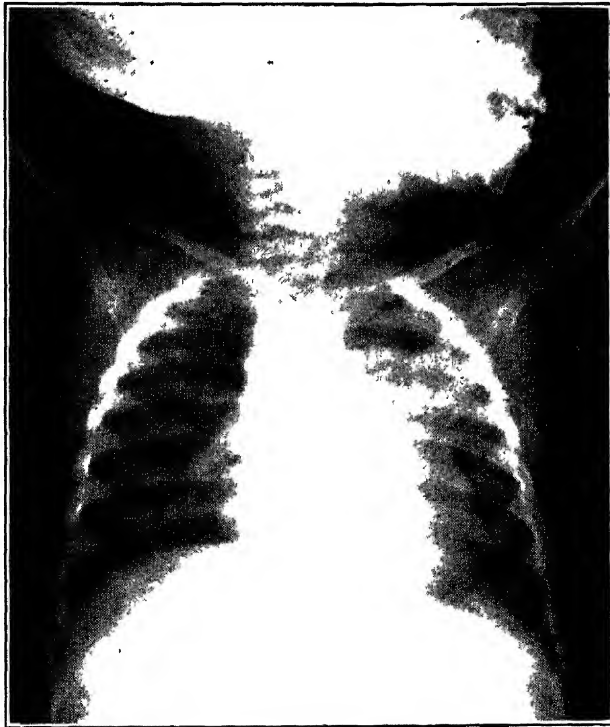


Fig. 4—Same case as Fig. 3, roentgenogram taken 7 months later. Shows beginning clearing (Mitchell and Nelson—Ohio State M. J.)

Reilly uses the Linzenmeier method which is carried out as follows

*Technic*—0.8 cc. of venous blood is drawn into a syringe containing 0.2 cc. of 5 per cent sodium citrate. After inverting the syringe, the mixture is introduced into a glass tube of 4 mm. diameter which has an 18 mm. mark below the level of the 1 cc. volume. The time taken for the cells to settle to the 18 mm. mark is noted. The normal range, variable with age, is as follows:

<i>Age.</i>	<i>Sedimentation Time.</i>
0 to 2 months	. May be as high as 10 hours
2 months to 2 years	. About 1½ hours
2 to 4 years	. About 2½ to 3½ hours
5 to 6 years	. About 2 hours
After 6 years.	. Gradual increase in time required until after 10 years of age, when females have a rate of 4 to 6 hours and males of 6 to 8 hours. After the sixth year of life a rate under 2 hours is always pathological.

*Prevention.*—Calmette's insistence that the B. C. G. bacillus is always acid-fast, and nonpathogenic has been questioned by Petroff and others. Numerous

other investigators have demonstrated that the tubercle bacillus during cultivation may pass through not only different forms, but may temporarily lose its property of acid-fastness. S. S. Sidenberg and E. E. Ecker (*Am. Rev. Tuberc* 29:571 (May) 1934) have demonstrated a nonacid-fast variant of B. C. G. in a culture obtained direct from Calmette in Paris. The variant possessed the growth properties of the tubercle bacillus and reverted to the acid-fast form when grown in various tubercle bacillus media over a sufficient period of time. None of the characteristics of a contaminatory organism were found in the variants. When injected into guinea-pigs cold abscesses were formed at the site of injection. Acid-fast organisms were recovered from these abscesses. This variant was devoid of pathogenicity for guinea-pigs.

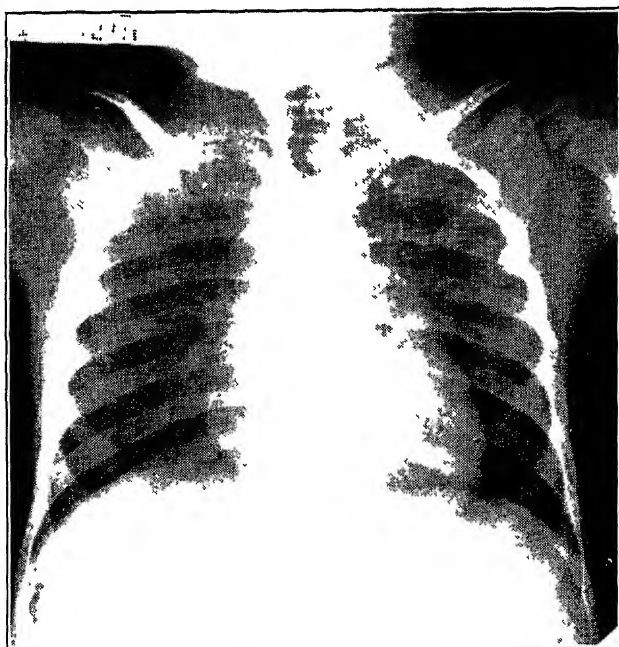


Fig. 5 — Same case as Fig. 3, roentgenogram taken 4 years later. Shows calcification in area of left upper as well as right hilus region. (Mitchell and Nelson, Ohio State M. J.)

J. Beerens (*Ann. Inst. Pasteur* 51:466 (Oct.) 1933) has made repeated injections of B. C. G. into guinea-pigs. In no instance was he able to increase the virulence of the B. C. G. organisms. He also placed sealed glass tubes containing respectively, virulent tubercle bacilli and B. C. G. into the peritoneal cavity of guinea-pigs. Morphological changes occurred more rapidly in the B. C. G. organisms. This is interpreted as evidence of the innocuousness of the B. C. G. injections.

Renewed interest in the possibilities of vaccination with heat-killed tubercle bacilli is bound to follow the recent work of S. A. Petroff, W. Steenken, Jr., and W. A. Winn (*J. Immunol.* 22:413 (June) 1932) and W. B. Soper, L. K. Alpert and M. J. Adams (*Am. Rev. Tuberc.* 28:667 (Nov.) 1933). Petroff showed that there was a difference in both the sensitizing and immunizing properties of dissociated, heat-killed, so-called "R" and "S" forms of avian tubercle bacilli. A greater hypersensitiveness was conferred in the chickens inoculated



with the "R" type and a greater immunity to subsequent infection with virulent avian tubercle bacilli by the "S" type but a lesser tuberculin hypersensitiveness.

Soper, working independently, compared the immunizing properties of dissociated, heat-killed, "S" bovine (B1) tubercle bacilli with those of B. C. G. and living human tubercle bacilli in the rabbit. Six weeks after vaccination each animal of the three groups and those of a control group were inoculated intrameningeally with identical doses of virulent bovine bacilli (B1). According to the results based on both survival and autopsy findings, the animals vaccinated with heat-killed "S" tubercle bacilli appeared the best protected. The animals vaccinated with living human tubercle bacilli and with B. C. G. were about equally protected. The results of these two investigations seem to suggest that there is a difference in the protective properties of heat-killed dissociated and undissociated tubercle bacilli and that the heat-killed "S" variant is more effective than heat-killed undissociated bacilli.

**SPONDYLITIS.—*Diagnosis.***—Because of the obvious benefits of early treatment of Pott's disease, R. I. Harris (Am. Rev. Tuberc. 29:223 (Feb.) 1934) emphasizes the need of early diagnosis. Since vertebral involvement is a potential possibility in each tuberculous patient, the physician should bear it in mind. Tuberculous spondylitis exists for varying periods of time before deformity is apparent. Diagnosis in this period is difficult but important. Harris says that the symptom most valuable for early diagnosis is spinal pain, which is increased by activity and weight-bearing, and relieved by rest, and which occurs not only in the diseased area, but is referred also to spinal segments corresponding in level to the diseased vertebræ. Other symptoms are muscle spasm, deformity, abscess formation, characteristic x-ray appearance and paraplegia.

**TUBERCULOUS MENINGITIS.—*Pathogenesis.***—A new concept of the pathogenesis of tuberculous meningitis has been presented by A. R. Rich and H. A. McCordock (Bull. Johns Hopkins Hosp. 52:5 (Jan.) 1933). It has been generally accepted that tuberculous meningitis results from a hematogenous distribution of tubercle bacilli from a preexisting focus and that it is frequently a part of a generalized miliary tuberculosis. The authors cite experimental and morphological evidence in support of their contention that diffuse tuberculous meningitis is not a direct and immediate result of hematogenous infection of the meninges, but that it has its origin in the discharge of bacilli into the cerebrospinal fluid from adjacent, older caseous tuberculous foci.

As arguments against the direct hematogenous route of infection they cite such objections as: (1) cases of miliary tuberculosis of extreme degree without meningitis, (2) cases of meningitis without miliary tuberculosis; and (3) lack of correlation between the age and character of the meningitis and of the miliary tubercles in other viscera in many cases in which meningitis and miliary tuberculosis do exist together.

The lining of the various serum cavities, pleura, peritoneum and pericardium stop and hold very little of any inert particulate matter injected into the circulation, and they are correspondingly little affected during miliary tuberculosis. It is the contention of the authors that the meninges behave in like manner. When,

during blood stream infection, tubercle bacilli do lodge in the meninges, only a small local reaction, at most, is to be expected with subsequent discrete tubercle formation at each site where bacilli have lodged

Experimentally, the authors have been unable to produce a prompt meningitis in either tuberculous or nontuberculous guinea-pigs or rabbits, by means of intravascular injection of virulent tubercle bacilli even when the injection was made into the carotid artery. Although all of the animals at autopsy had more or less extensive visceral miliary tuberculosis, only 2 of 40 animals had any lesions whatsoever remotely suggestive of exudative meningitis. Small circumscribed tubercles were frequently found in the brain substance, more rarely in the meninges, and several times tuberculosis of the choroid coat of the eye was found. In one of the two instances of diffuse exudative meningitis, the origin was shown to be from a focus in the eye.

Since acute diffuse tuberculous meningitis is characterized especially by its exudative inflammatory nature and since such a reaction is an expression of the allergic state, the authors do not believe that a sufficient number of tubercle bacilli are deposited in the meninges during the course of a hematogenous infection to produce such a violent allergic reaction.

Because of the doubt cast upon the hematogenous route of infection, reëxamination of the available pathological specimens from patients dying of tuberculous meningitis was made in search for contiguous caseous tuberculous foci. Such discharging foci were found in the substance of the brain or cord, in the meninges, in the bones encasing the central nervous system, or in the choroid plexus in 77 of 82 cases examined. In all but 2 of these 77 cases the demonstrated source of the diffuse meningitis was situated in the substance of the central nervous system or in the meninges. In the 5 cases in which no local focus was found, the material for study was incomplete. Thus, the authors conclude that tuberculous meningitis has its origin in the discharge of bacilli into the cerebro-spinal fluid from adjacent, older caseous tuberculous foci.

**WHOOPING COUGH (PERTUSSIS) — *Epidemiology.***—The *seasonal occurrence* of whooping cough in 29 states of this country was analyzed recently by G. E. Harmon (Am J Pub Health 23: 789 (Aug) 1933). Three years of greatest incidence were compared with 3 years of lowest incidence. During epidemic years a certain group of states, mostly of the northern section of the country had seasonal peaks in March or April. Another group of states, including both southern and some northern states, had peaks later than April. *Geographic location* seemed to have no definite bearing on the time of greatest incidence of this disease. October was generally the month of lowest incidence of pertussis in years of high as well as in years of low incidence. During the years in which whooping cough was less frequent, the peak of the incidence came slightly before, during, or slightly after the peak of the great epidemic years, varying in different states, with no relationship to that state's location and climatic conditions.

The occurrence of whooping cough in *old age* is uncommon, but has been reported occasionally in the medical literature. A. J. Hall (Proc. Roy. Soc. Med.

26:1146 (July) 1933) observed 2 interesting cases of this sort in elderly persons. One was a physician 72 years of age, who had no recollection of having had the disease in early childhood. During 40 years of practice he had been exposed to the disease many times and had not contracted it. Another patient, a woman, 73 years of age, contracted whooping cough. She had had previous exposures also and many years before had taken care of her child who died during an attack of the disease. Other instances of whooping cough in patients of advanced years were cited by the author who concluded that (1) the possibility of whooping cough should be borne in mind in every case of prolonged paroxysmal coughing when no other etiologic factor can be discovered, and (2) the immunity of adults to the disease, whether or not they have had previous attacks, may not always be assumed to be permanent.

**Etiology.**—Some investigators have questioned the evidence that the *pertussis bacillus* is the sole cause of whooping cough. In order to determine the rôle played by this bacillus in the etiology of the disease, H. MacDonald and E. J. MacDonald (J. Infect. Dis 53:328 (Nov-Dec) 1933) inoculated 4 boys with pure cultures of the microorganism. Two of these boys had been vaccinated by the method of Sauer 5 months previously, the other two had not. None had had whooping cough previously. Nasal instillation of a filtrate of the culture did not produce any symptoms of whooping cough during a period of 18 days in any of the 4 patients, but the inoculation of the noses and throats with a suspension of the microorganism produced symptoms of the cough within 7 days in the 2 unvaccinated boys. They developed typical symptoms and signs of the illness with characteristic leukocytic reactions. The 2 vaccinated boys remained entirely free of symptoms during the same period of time.

**Intranuclear inclusion bodies**, which have been found in the lungs of 45 per cent of 40 children who died of pertussis, by H. A. McCordock and M. G. Smith (Am J Dis. Child. 47:771 (Apr.) 1934), occur usually in the diseases having a virus as their etiologic agent. These inclusion bodies were also found in the salivary glands of 4 of a group of 6 pertussis patients. Similar bodies have been found in the salivary glands of 10 per cent. of patients dying from other diseases than whooping cough. The authors concluded that intranuclear inclusions in whooping cough might be due to (1) an activation of a latent or secondarily invading virus; (2) the occurrence of a disease which resembled whooping cough but was caused by a virus, (3) the presence of more than one virus which in various diseases produced the same type of lesion, and therefore the lesions in whooping cough resulted from the action of a "pertussis virus", (4) a specific virus having a definite relation to whooping cough infections.

The *pertussis bacillus* has been accepted as the etiologic agent of whooping cough by M. Gundel and W. Schluter (Klin Wchnschr. 12:1633 (Oct 21) 1933) and they were convinced that the methods of identification of the *B. pertussis* and the differentiation of it from other types of bacilli were satisfactory. Besides the characteristic morphology and cultural behavior, the identification was established by skin tests on guinea-pigs. Injections of the pertussis bacillus cultures caused severe necrosis while the influenza bacilli produced only an erythema and infiltration. Last of all, if necessary, complement fixation reac-

tions with guinea-pig immune serum or with human convalescent serum of whooping cough patients were found specific for the detection of the specific microorganism.

**Diagnosis.**—The *cough plate method* of diagnosis of whooping cough has been used extensively by the Public Health Department of Grand Rapids. The plates were exposed by the district nurses in all cases of suspected whooping cough, chiefly among the poorer classes receiving relief. In the report of the results of this work, P. Kendrick and G. Eldering (Am. J. Pub. Health 24: 309 (Apr.) 1934) mentioned the value of early diagnosis both to the patient in respect to treatment and to the health officials in instituting early isolation. The diagnoses could be made within 48 hours in 23 per cent. of cases, within 72 hours in 75 per cent., and in 4 days in 91 per cent. The procedure proved to be a much more accurate method of diagnosis of carriers; of the length of time the patients harbored the bacilli; an aid to the determination of recurrent attacks of the disease and the diagnosis of doubtful coughs and respiratory infections. B. Kristensen (J. A. M. A. 101: 204 (July 15) 1933) employed the cough plate method of isolation of the bacillus, and cultures were also obtained from the pharynx by means of a curved probe when the patient's coughing period ceased. Of 109 children studied from week to week, only 7.5 per cent. harbored pertussis bacilli after the fourth week of the convulsive stage and after the tenth week no bacilli could be found.

Investigating the question of whooping cough *carriers*, the author made cultures of 500 normal persons not exposed to the disease, 301 persons who had been in close contact with pertussis patients for a week, and 202 patients suffering from other diseases. The microorganisms were found only in 9 of the group who had been exposed directly. All 9 of these patients subsequently contracted the disease. In the examination of 80 families in which one or more members had pertussis the author detected 40 instances of children under 15 years of age who had abortive whooping cough. These children had positive pertussis cultures, had been exposed to the disease, and had had protracted atypical coughs over a period of a month. Four adults had similar attacks. Such forms of the disease were thought to occur frequently and constitute an important factor in the dissemination of the infection.

Studies of the *leukocytic reaction* and the *sedimentation rates* of the blood of whooping cough patients were found to be of some value in diagnosis by D. Moritz and L. Lackner (Arch. de méd. d. enf. 36: 669 (Nov.) 1933). In a group of 65 such patients, 45 of whom had uncomplicated infections, the increase in the total number of leukocytes and in the absolute number of lymphocytes was found to be quite characteristic except in very early stages of the disease. During this early period, several examinations of the blood were found to be necessary before any diagnostic value could be attached to the procedure. In uncomplicated cases of whooping cough, the sedimentation rates, determined by a micro method, were normal in 55 per cent., decreased in 25 per cent., and elevated in 20 per cent. All of the patients with complications, however, had increased sedimentation rates and a shifting of the leukocytic hemogram to the left. It was concluded that an elevation of the absolute number of lymphocytes above 10,000 and a

decrease in the sedimentation rate was indicative of whooping cough, although the absence of these signs did not exclude the diagnosis. After a study of the blood picture in several patients with whooping cough, I. Inaba (Ztschr. f. Kinderh. 55:677 (Dec.) 1933) concluded that the lymphocytosis follows very closely the reaction of the body to the infection with the pertussis bacillus, increasing as the paroxysms become more severe and declining as the cough subsides. Therefore, the diagnosis of the disease may be determined with a fair degree of accuracy if two or more examinations of the blood are made at intervals of a day or more. Any decrease in the total count tends to rule out the presence of pertussis unless made during the catarrhal stages of the disease. Relapses of the disease were shown to be rare, but an exacerbation of the cough occurred as the result of non-specific factors. V. B. Dolgopol (J. Pediat. 3:367 (Aug.) 1933) had an opportunity to observe the leukocyte count in 5 children for several weeks before the onset of whooping cough. With the normal level of their total leukocyte counts for comparison, the author noted that there was no increase in the count or in the percentage of lymphocytes during the catarrhal stage of the disease, but with the onset of the paroxysms there was a sharp rise, especially of the total number of leukocytes. The lymphocyte count remained high during bronchitis, which occurred in a complication of the disease. At no time was there any reduction in the absolute number of neutrophils and sometimes there was an increase. Leukocyte counts expressed in percentages and in whole numbers of cells per cubic millimeter of blood gave more information concerning the nature of the disease than just the percentages alone.

**Complications.**—A large group of children who had had whooping cough recently were kept under observation for a period of 3 years by E. Gabriel (Jahrb. f. Kinderh. 142:281 (May) 1934) in order to determine the occurrence of *tuberculosis* as a complication of the pertussis. Of the total group of 1995 patients, 359 or 18 per cent, who were children of the youngest age groups, died during the acute stages of the disease. A total of 915 were discharged from the hospital as cured. The remaining number, 721, were not entirely well when they left the hospital against the physicians' advice, and of this last group, 491 patients were observed over a period of several years. There were 26 deaths among these patients after they had left the hospital and 7 of the deaths were caused by tuberculosis. The patients who died of tuberculosis constituted 1 per cent of the group observed during the 2 years after their release from the hospital and 0.4 per cent of those observed longer than the 2-year period. This mortality rate was high in comparison with that of the healthy child population, but compared with the mortality rates of children who were convalescent from other illnesses of the respiratory tract, it seemed quite low. Children who had evidence of tuberculosis at the time of onset of the whooping cough had very little evidence of exacerbations of their tuberculous lesions during their acute illness.

In reviewing the relation of *convulsions* to whooping cough, H. Grenet and E. Mourrut (Arch. de méd. d. enf. 36:585 (Oct.) 1933) have found certain predisposing factors which seemed to influence the complications. They noticed waves of increased incidence of convulsions and the last one in their locality had occurred within the last 2 years and included 22 cases of convulsions among 238

hospital patients with whooping cough, a proportion of about 1 in 10. The age of the patients seemed to be important, since all but one of the 22 patients were less than 3 years old. The severity and number of paroxysms of the pertussis infection had no apparent influence on the occurrence of convulsions, but other complications, especially the pulmonary lesions and otitis media, frequently led to convulsions. Two or three days before the occurrence of convulsions the children often appeared stuporous or restless and had a rise in temperature. After the convulsions, the patients occasionally had some residual paralysis, such as a hemiplegia or ocular muscle paralysis, but generally the neurologic examination was negative and there were rarely any signs of meningeal irritation, and the cerebrospinal fluid was generally normal. The time at which the convulsive seizures occurred and their duration bore no relation to the stage of the disease or its complications. Patients with this symptom frequently died and among the above series of 22 cases, 20 or 87.5 per cent were fatal.

From the postmortem examination of 15 patients the authors observed that (1) meningeal or cerebral hemorrhages were rare and the cause of the convulsions was definitely not a mechanical one; (2) a certain number of patients had encephalitic lesions; (3) degenerative lesions, as described by some pathologists, occurred in rare instances, (4) the majority of patients had only a congestion and edema of the brain and some had no evidence whatever of pathologic changes. It was the conclusion of the authors that the convulsions were caused by a toxin rather than by any mechanical, allergic or bacterial agent.

*Encephalitis* following whooping cough was observed by A. Santillana (*Ibid* 36: 474 (Aug.) 1933) in 2 children, 22 and 19 months of age. The symptoms of encephalitis, which began 2 months after the onset of pertussis, consisted of somnolence, convulsions and alterations of muscle tone. The cerebrospinal fluid showed no evidence of any other specific lesion. Both children died, one of spasm of the glottis, the other from the brain lesion itself.

Several *neurologic* complications of whooping cough have been observed recently. One such patient who developed blindness as the most striking feature was seen by S. D. Lazarus and G. Levine (*Am. J. Dis. Child* 47: 1310 (June) 1934). This boy, 6 years of age, developed symptoms of blindness of both eyes in the fourth week of his illness. The pupillary reflexes were absent and the optic discs were choked. Later there was a right hemiplegia, aphasia and drowsiness, but during the next 3 months the entire condition improved greatly. A toxic hemorrhagic encephalitis with cerebral edema was thought to have been the underlying pathologic condition in this instance. In the medical literature 20 similar reports of blindness in pertussis were found and in more than half of the cases mention was made of evidence of some intracranial lesion. The optic neuritis cleared up in 3 days to 9 months in all but 2 of the patients. An instance of *paraplegia* with extreme flexion of the legs was reported by F. Pichon and H. Cambessédès (*Arch. de méd. d'enf.* 37: 33 (Jan.) 1934). Their patient, who was a child 3 years of age, developed symptoms about 3 weeks after the onset of whooping cough and died 3 weeks later. The cerebrospinal fluid was normal. Autopsy was not permitted so that the exact location of the lesion was not determined.

An unusual complication of whooping cough, described by J. M. Frawley (Am. J. Dis. Child. 46: 346 (Aug.) 1933), occurred in a child, 2 years of age, who developed signs and symptoms of *intestinal obstruction* during the third week of pertussis. At operation, the *gastrocolic omentum* was found *ruptured* and the stomach had protruded through it, causing obstruction to the passage of fluid or food. A condition of ileus developed and death occurred 24 hours after operation.

**Treatment and Prophylaxis.**—An antigen prepared from the endotoxin of pertussis bacilli is an effective therapeutic agent in the treatment of whooping cough, according to J. M. Frawley, M. Stallings and V. C. Nichols (J. Pediat. 4: 179 (Feb.) 1934). The bacilli were macerated in a ball mill, washed and filtered. The filtrate contained the extract from about 12 billion pertussis bacilli. The initial dose of this material was 0.1 c.c. intradermally and 0.1 c.c. subcutaneously. Increasing amounts were given subcutaneously each day until 1.0 c.c. was being administered. Occasionally 0.25 c.c. was given every other day until the dosage reached 1.0 c.c.

Of a group of 35 patients exposed to the disease and treated in the above manner, 14 did not develop any symptoms of the disease. It was thought possible that these children had not been sufficiently exposed or were immune. Of the remaining 21 of the group, 76 per cent. had very mild attacks of the disease, 14 per cent. had a fairly mild course, and 10 per cent. did not seem to be benefited at all by the treatment.

Another group of 86 patients received the treatment during the first week of their catarrhal symptoms and of these, 69 per cent. had a definitely favorable response, 19 per cent. improved somewhat, and 12 per cent. had no favorable changes. In a third group of 79 patients treated later than one week after the onset of the symptoms, 45 per cent. reacted favorably, 43 per cent. fairly so, and 12 per cent. not at all. There was little or no local constitutional reaction to the injected material.

In a subsequent report, J. M. Frawley (*Ibid.* 4: 184 (Feb.) 1934) described the results of active immunization of a group of school children with the same antigen. A group of 345 children of the early school grades who had not been exposed to pertussis previously received an initial dose of 0.1 c.c. intradermally and subcutaneously and a similar dose a week or two later. The third and fourth injections, consisting of 1.0 c.c. subcutaneously were given at intervals of 1 to 2 weeks. Mild local reactions appeared in 6 to 8 hours and disappeared by the end of 24 hours. A group of 614 children of the same ages and environment constituted a control group. During succeeding months the disease was contracted by 42 of the treated group and 60 of the control series. In the group of vaccinated children, 88 per cent. had mild or moderate attacks, 14 per cent. severe attacks. Among the controls 55 per cent. had mild or moderate forms of the disease and 45 per cent. had severe infections. Although the treatment had not reduced the incidence of the disease, the authors felt that the severity was considerably modified.

A vaccine prepared by Langer was employed successfully in the early treatment and prophylaxis of whooping cough by E. Kruger (Deutsche med. Wchnschr. 60: 741 (May 18) 1934). This vaccine was made from 58 strains of

pertussis bacillus from which the endotoxin had been extracted. It was thought that the bacterial proteins were the essential factors in the prevention and treatment of the disease because of their production of lysins in the patient. When the vaccine was administered in the early stages of the disease in 42 children, the course and severity of the attack seemed to decline. Of a group of 10 children exposed to the disease, 7 were protected by prophylactic injections. The dosage was 5, 10, 15 and 20 billion organisms, respectively, in 4 successive intramuscular injections. Reactions were mild, although a few children developed a slight fever.

T. Madsen (J. A. M. A. 101:187 (July 15) 1933) reported the results of the treatment and prophylaxis of whooping cough in the Faroe Island by Zachariassen. In these islands epidemics of this sort occur at rather long intervals and are, therefore, unusually suitable for testing prophylactic and therapeutic measures. In the epidemic which occurred in 1923 and 1924, 2094 patients were given prophylactic injections of the vaccine and 627 were not treated. Most of the persons in both groups contracted the disease so that the vaccine was of little value in checking the epidemic. However, the severity of the disease in the untreated group was much greater and the mortality was 12 times greater than in the treated group.

Another whooping cough epidemic occurred in 1929. At this time 1832 individuals were given prophylactic injections of the vaccine and 446 were not. In the treated group 458 avoided the disease entirely, while all but 8 of the untreated group contracted pertussis. The number of severe cases and the mortality were much greater in the group which had not received the vaccination treatment.

These favorable results obtained with vaccines in the Faroe Islands were attributed to (1) freshly prepared vaccine from young strains, (2) large doses of about 22,000 million bacteria, and (3) the completion of the vaccination treatment shortly before the epidemic started.

In the author's experience in Denmark, reactions to the vaccine did not appear to be severe. There were 2 instances of newly born infants who died suddenly after the second injection of vaccine. Whether or not this was due to the treatment was difficult to determine, but since this occurrence, prophylactic vaccine treatment of infants under a month old has been avoided.

The successful prophylactic use of specially prepared **Sauer vaccines** which have been adopted recently by many clinicians, has been reported by L. W. Sauer (J. A. M. A. 101:1449 (Nov. 4) 1933). He now has a group of 479 children of ages of 8 to 28 months who have received the injections of vaccine and have escaped the infection although several epidemics have occurred in the community. From 7 to 8 c.c. of his vaccine, containing 10 billion bacilli per c.c. in all, were found to protect the infant or child if the injections were completed 4 months or more before the patient was exposed to the disease.

In the experiments of MacDonald (*loc. cit.*) mentioned above, vaccination of 2 boys with **pertussis vaccine** protected them against subsequent nasal and pharyngeal inoculations of pertussis bacilli.

The potency of the antigen of various preparations of whooping cough vaccines and saline extracts was studied by J. J. Miller (J. Immunol. 26:247 (April)



1934). The complement fixation reaction of rabbits was used as the measurement of the antigenic power of the material. Freshly prepared extracts of recently isolated strains of the pertussis bacillus seemed to cause a more rapid antibody formation than did vaccines. The antigen was adversely affected by the addition of formalin, chinisol and tricresol. The extracellular bacterial substance apparently represented the antigenic factor and was relatively heat stable.

The treatment of whooping cough with **immune adult serum** was tried by I. Jundell (Acta. paediat. 15:1 (Sept.) 1933) in 23 patients who had been exposed to the disease. In one group of 10 who were treated during the incubation period of the disease, 8 did not contract the illness and 2 had very mild attacks. The other group of 13 children received the first injection during the early paroxysmal stages of the disease and the course of the illness seemed to be favorably influenced in every instance.

Subsequently, serum was collected from adults who had had whooping cough in childhood and had recently received 3 subcutaneous injections of pertussis vaccine. This serum was given to 3 children in the incubation or catarrhal stages of the disease and to one in the early part of the paroxysmal stage. A control group consisted of twin brothers or sisters of the patients in 2 instances and older children of the same family in the 2 other cases. Considerable amelioration of symptoms occurred in the treated group. A dosage of 60 to 80 c c of the serum given intramuscularly or subcutaneously at intervals of 2 to 4 days was thought necessary.

The *degree of immunity* conferred to the patients treated with pertussis vaccines was determined by A. Kairies and S. Goetze (Ztschr. f. Kinderh. 55:551 (Oct.) 1933). Complement fixation reactions with pertussis bacilli were positive in all but one of a group of 14 children who had had whooping cough. These antibodies could not be demonstrated in the blood of 4 healthy infants who had not had the disease, but had been vaccinated against pertussis. In children over a year of age who had received pertussis vaccine, complement fixation bodies were found on the eighth day after the first injection, reached their maximum amount on the tenth to twenty-fifth day, and in 4 instances, disappeared at the end of 5 weeks after the initial treatment. Vaccination therapy seemed to be successful when it was begun during the first week of the paroxysmal stage of the disease or earlier. Children with allergic reactions or other infections responded poorly to vaccination and often had falsely positive complement fixation reactions. The serum of vaccinated children occasionally gave positive reactions with antigens of the Wassermann test and those of *B. coli*, staphylococci and influenza.

*Skin Tests of Immunity*—A cutaneous reaction as a method for the determination of a patient's immunity has been devised by S. K. Siebler and S. Okrent (J. Pediat. 4:188 (Feb.) 1934). One or 2 minims (0.06 or 0.12 c c) of a suspension of the pertussis bacilli killed with 0.5 per cent phenol were injected intracutaneously in a group of 186 patients and readings were made at the end of 72 hours. An erythema 10 c mm or greater in diameter at the site of injection was considered as a positive reaction. Among those who had not had pertussis previously, 80 per cent had positive reactions, while 76 per cent of those who had the disease gave negative reactions. In 4 instances children with negative

reactions were subsequently exposed to the disease but did not contract it. Control tests with phenol solutions and with stock vaccines gave no comparable reactions

Similar skin tests with 3 types of material were tried by N. B. Krarup (*Compt. rend. Soc. de biol.* 115 85, 1934). The first substance was a killed culture of gray pertussis bacilli in saline solution and 0.5 per cent. phenol, the second was a similar mixture of green types of the bacillus, and the third preparation consisted of the same type of microorganisms subjected to autolysis by heating the mixtures to 37° C for 3 days, cooling for 2 days, heating for 1 more day at 27° C., and then removing the bacteria by centrifugation

Skin tests with these 3 mixtures were made in a group of 14 patients who had not had pertussis; in a group of 13 who had had the disease previously; and in a group of 8 infants in the convulsive stages of the disease. There was no significant variation in the reactions of the 3 different groups of children and the results with the different bacterial materials were indefinite.

# NEUROLOGY AND PSYCHIATRY

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### **NEUROLOGY.—BRAIN TUMOR.—*Frequency of Headache.*—**

Among patients suffering from brain tumors, severe *headache* occurs most commonly when the neoplasms are in the temporal, suprahypophyseal, and pontine regions, according to F. A. Gibbs (*Arch. Neurol. and Psychiat.* 31: 152 (Jan) 1934). It is least frequent when the growths are in the midbrain or in the caudate nucleus area. This distribution of the frequency of headache as correlated with the site of the tumor, closely follows the corresponding curve for generalized convulsions as a symptom of brain tumor. On the other hand, the frequency distribution of choked disc and projectile vomiting were so different from the data for headache as to negate the possibility that choked disc, headache, and vomiting were all due to the same cause (increased intracranial pressure). The close similarity in the distributions of the data for headache and for convulsions lends strength to the hypothesis which would relate migraine with epilepsy. That headache and convulsions are more frequent when the tumor is at the suprahypophyseal, pontine, and temporal area suggests that this might be due to the distribution of the neural elements concerned along the cerebral arteries, concentrating, therefore, at the base of the brain.

**PARASELLAR TUMORS.**—A small group of brain tumors arise from the sphenoid ridge; these growths, usually fibroblastomata, are little understood. B. J. Alpers and R. A. Groff (*Ibid.* 31: 713 (Apr.) 1934) report 8 cases of this type, 4 lying medially on the ridge, 4 laterally. The characteristics of the two forms differ somewhat, those of the lesser wing (medial to the ridge) exhibiting a much clearer and more consistent clinical symptomatology than growths of the greater wing (lateral to the ridge). Tumors of the former class are confined to the lesser wing, and are thus in intimate contact with the sella and the associated neurovascular structures. The clinical syndrome includes: visual field cuts (usually, hemianopic; occasionally, quadrantic), primary optic atrophy, third nerve involvement, and unilateral impairment of the first nerve. Slight erosion of the dorsum sellæ and anterior clinoids is often noted by the x-ray. Tumors of the greater wing, on the other hand, present no such clearly defined syndrome. The visual fields are likely to be normal, and the first and second cranial nerves may or may not show impairment of function. Papilledema associated with secondary optic atrophy on the tumor-side may be noted. Some erosion of the sella or of the roof of the optic foramen may be visualized by x-rays in some cases. Unilateral exophthalmos on the side of the neoplasm may occur, and when it is found, is strongly suggestive of greater-wing tumor.

**CEREBRAL DIPLEGIA.—*Etiology.*—*Birth Injury*** — According to T. D. Gordon (*J. Michigan M. Soc.* 32: 165 (Mar) 1933), it is inconceivable that intracranial hemorrhage could cause so many deaths in the newborn and not cause permanent damage to the brains of a considerable number of patients who survive. Probably very few children are born without some injury. As the cerebral cortex is not functioning at birth, there may be considerable damage to the brain without very definite clinical signs. The signs of birth injury usually pass off in from 2 to 4 weeks and the child is considered normal until the age of

7 to 12 months The latent period in cerebral diplegia is very important Intra-cerebral hemorrhages are more important than meningeal hemorrhages The author does not believe cerebral diplegia to be the result of an arrest of development of the pyramidal tracts due to prematurity. Primary neuromic degeneration from some unknown cause is considered a very vague theory. He believes that many cases of cerebral diplegia may be prevented by skillful, unhurried obstetrics, gentle resuscitation, and better cooperation between the obstetrician and the pediatrician.

**CEREBRAL HEMORRHAGE.**—*Treatment.*—Patients with cerebral hemorrhage, whether the condition be traumatic or apoplectic, will be greatly benefited by **autohemotherapy**, according to R. Colella and G. Pizzillo (*Rassegna internaz. di clin. e terap.* 15: 386 (Apr. 15) 1934), who have studied this form of therapy in a large series of cases. They remove 25 or 30 c.c. of blood from the cubital vein and reinject it immediately into the gluteal musculature of the patient. It may be necessary to citrate the syringe to prevent clotting. Because of the frequently poor tone and nutrition of the paralyzed buttock, it is advisable to make the injection into the healthy gluteal side. The exact mechanism is not understood, but Colella and Pizzillo are inclined to believe that the favorable action of the reinjected blood is due to its hemostatic qualities. Patients with cerebral thrombosis do not respond as favorably to this autohemotherapy as do those with cerebral hemorrhage. Sufferers from head injury and consequent intracranial bleeding are usually relieved rapidly by this technic, which appears to lower the intracranial vascular pressure. For this reason, the procedure is also recommended as a form of prophylaxis in hypertensive patients in whom a stroke is anticipated.

**CONVULSIONS.—NARCOLEPSY.**—Narcolepsy is not a disease, but a group of symptoms. This syndrome may occur under varied conditions, 5 such groups of conditions are classified by John Notkin and S. E. Jelliffe (*Arch. Neurol. and Psychiat.* 31: 615 (Mar.) 1934), and each type is illustrated by case reports. These groups are: (1) Neurotic and psychotic instances of hypersomnia in hysteria, manic-depressive insanity, dementia precox, etc.; (2) encephalitic; (3) somatic conditions other than encephalitis, illustrated by an instance of narcolepsy in conjunction with dementia paralytica; (4) associated with epilepsy; and (5) idiopathic, *i. e.*, cases with nothing to associate them with any specific condition. Of these 5 classes, the last is the most common, 270 cases of idiopathic narcolepsy having been counted by the authors in a review of the literature. The second commonest type is the somatic (nonencephalitic) group, represented by 88 cases collected from the literature. The most uncommon form is that associated with epilepsy, only 30 cases of this sort being reported. In spite of the infrequency of this association, the authors are inclined to classify narcolepsy as a syndrome closely related, physiologically and pathologically, to the epileptic state. The paroxysmal and periodic nature of the two states is the most conspicuous point of similarity between them, but many other suggestive items of similarity are listed. The so-called "cataplectic" spells are found only in the idiopathic form of narcolepsy.

Stressing the close anatomic relationship between the sleep and heat-regulating centers, Heinrich Reinwein (Deutsche med. Wchnschr. 60:1382 (Sept. 14) 1934), points out that *disturbances in the heat-regulating mechanism* should be expected in cases of narcolepsy. This, he illustrated by 2 cases. Both of these patients had suffered from head injuries, and both had cerebral tumors. One of the patients showed a pituitary type of baldness; the other, an acromegaly. The disturbances in heat regulation in each case took the form of a discrepancy between rectal and axillary temperatures. In most instances, the rectal reading exceeded the axillary by more than the usual  $1^{\circ}$ , but many times, the axillary reading was actually above that at the rectum. Cases of narcolepsy with hypothermia, reported in the literature, are recalled. To explain the dysthermia, the author suggests 2 hypotheses: (1) Impairment of hypophyseal function with disturbance in hormone balance, and (2) morphologic changes in the brain itself.

**EPILEPSY.—Etiology.**—Jonathan Forman (Arch. Neurol. and Psychiat. 32: 517 (Sept.) 1934) points out that *atopy* (by which he means that form of allergy controlled by inheritance) is the cause of a small but definite number of cases of "idiopathic" epilepsy. Edema of the tissues and spasm of smooth muscles are well-known allergic responses and it is not surprising that allergic conditions should occasionally produce generalized convulsions. To recognize a case of atopic epilepsy, 3 criteria must coexist: (1) A history, either in the patient or his family, of an allergic disorder such as hives, asthma, vasomotor rhinitis, etc.; (2) eosinophilia, especially just before or during a paroxysm; and (3) positive reactions to skin tests. If the case appears, on the basis of the first two criteria, to be atopic, the offending substance may be identified by skin tests and by clinical trial. By clinical trial, Forman means (1) removing the specific excitants or (2) raising the tolerance by injections of the substance in small but graduated dosage. Skin tests may be performed on the patient by means of either the scratch or intradermal techniques. Patch tests should not be employed. Tests may also be performed on a normal person previously treated with some of the subject's serum (the indirect or Walzer method).

When an allergy has been established, *treatment* should consist of (1) removing the excitant, (2) increasing tolerance by gradual introduction of the offending substance, (3) by removing or diminishing the secondary and nonspecific factors, such as changes in temperature, emotional disturbances, etc., (4) and by changing the physico-chemical balance, as may be done by therapeutically overcoming alkalosis, or by administering vitamin "A."

Ten cases are reported, in 1, the patient had had only a single attack, 1 was a case of *petit mal*, and 8 were instances of *grand mal*. The patient with *petit mal* was sensitive to chocolate, eggs and cabbage, and was promptly, and apparently completely, relieved by an **elimination diet**. In 8 *grand mal* cases, the substances to which they were sensitive and the results of treatment were: (1) Sensitive to potatoes, fish and milk, free from seizures on an elimination diet. (2) Wheat, rice, milk, eggs, peas and mustard. No spells except when patient included these in his diet. (3) Cabbage, tomatoes and beans, relieved when these were eliminated, occasional subsequent attacks, usually explained by inclusion of one of these in diet. (4) Many positive findings on skin test, but

patient refused to follow program and no improvement was reported (5) Cornmeal, mackerel, rice, wheat, house-dust, and goose-feathers Relief was obtained as long as the patient followed diet (6) Sensitive to a great many foods, but patient refused to follow therapeutic régime; no improvement. (7) Dog dander, feathers, wheat, oats and spinach; avoidance of inhalants and elimination diet brought about complete relief. (8) Beans, apples, peppermint, mackerel, milk An elimination diet resulted in cessation of attacks.

In the small proportion of cases due to atopy, Forman points out, seizures will not occur if the patient can be kept from the offending materials

In the study of a series of 42 patients who were subject to generalized convulsions with unconsciousness, Frank Fremont-Smith (A. J. Psychiat 13:717 (Jan.) 1934) found a direct relationship between the spell and *emotion* in 31 cases Eighty-four per cent of the patients, therefore, showed this relationship at some time. The emotions which seemed particularly prone to precede a paroxysm were fear, guilt, and frustration. In some cases, even a discussion of the emotion precipitated, or at least preceded, the attack In a few cases *pain* and *cold* seemed to bring on a spell, suggesting an association with the sympathetic nervous system In susceptible patients, the onset of *acute infections* has occasionally precipitated a seizure. The time relationship and, if any, the causal relationship, between the emotion and the spell, were often reduced by **psychotherapy**.

In analyzing the case records of more than 1300 pairs of *twins*, A. J. Rosanoff, L. M. Handy and I. A. Rosanoff (Arch Neurol and Psychiat. 31. 1165 (May) 1934) found 107 instances of epilepsy in both members of the pair. Of the monozygotic twins with epilepsy, only 1 was affected in 39 per cent of the cases, of the dizygotic twins, the convulsive disorder affected only a single member in 76 per cent of the cases From this analysis 3 conclusions may be reached (1) Since both members of the pair were affected more often (61 per cent compared with 24 per cent) in monozygotics than in dizygotics, some hereditary or germinal factor exists in the development of a tendency towards convulsions, (2) hereditary factors, by themselves, are inadequate to precipitate the convulsions clinically, since in the case of monozygotic twins, one of the members of the pair escaped in more than a third of the cases, (3) hereditary factors are not indispensable, since in a large proportion (24 per cent) of the cases in dizygotic twins, both members of the pair were affected, although the heredity was not identical

Epilepsy seems closely related to certain other neuropathologic conditions, such as Little's disease, Jacksonian fits, stammering, alexia, left-handedness, and mental deficiency Family histories often show several of these conditions in one family-tree

The authors are inclined to stress the importance of *brain trauma* as a factor in convulsions They point out that epilepsy and mental deficiency occur with disproportionate frequency among the first born, who are, of course, likely to be subjected to greater birth trauma than their younger siblings It is not the direct or compressing force of the trauma which seems to produce the cerebral lesion, so much as the compensatory extension which takes place at



right angles to the compressing force. Brain tissues are better able to tolerate compression than extension. The skull of the infant is more flexible than that of the older child or adult, and injury applied in infancy, therefore, is more likely to produce this compensatory extension than an application of the same force to the more rigid skull of the adult. The epileptic syndrome in traumatic cases is determined not by the severity or extent of the original injury to the brain, but by its localization and by the nature of the tissue reaction in response to the primary trauma. Slight trauma, the authors stress, may precipitate or initiate changes ultimately resulting in a convulsive state.

A case of epilepsy in a pair of monozygotic female *twins*, 8½ years old, is reported by D. E. McBroom and R. C. Gray (*Ibid.* 31:824 (Apr.) 1934). A maternal aunt had had epilepsy, but the family history was otherwise clear. The twins had a common placenta and were born prematurely. The development in early childhood was normal, the first born, "A," being somewhat ahead of the second born, "B," in development. Neither twin ever had any convulsions until the age of 5, when "A" had a seizure. A week later "B" had her first spell. Thereafter, seizures continued to increase in frequency, ultimately necessitating commitment to a colony. At the institution it was noted that "A" had about 3 *petit mal* spells a day; she did not suffer from *grand mal*. "B" had about 30 attacks daily, some of which were of *grand mal* type. At the age of 6, each twin had an I. Q. of 95; at the age of 8½, "A" had an I. Q. of 85, and "B" of 87. Dental, Bertillon and biochemical measurements stressed the great similarity between the two girls. The concurrence of idiopathic epilepsy in monozygotic twins is rarely reported and is of considerable genetic importance in strengthening the hypothesis that the convulsive tendency is an inheritable trait.

*Vascular spasm and cerebral anemia* have for a long time been advanced as the physiologic causes of epileptic spells. This hypothesis, although plausible and highly accepted, appears to be incorrect. F. A. Gibbs, W. G. Lennox and E. L. Gibbs (*Ibid.* 32. 257 (Aug.) 1934) have measured the rate of blood flow in the jugular veins of epileptic patients by means of a hollow needle with an electrically heated tip, and a thermocoupled stylet which recorded the difference in temperature between the tip and the stylet. The faster the blood flows, the cooler the tip becomes.

In one case, the blood flow increased rapidly a few seconds after the first tonic contraction. During the spell, the blood flow remained at a constantly high level. In another, there was a sharp decrease in the cerebral blood flow immediately after the onset of the paroxysm. This decrease, occurring after the attack had begun, could not, of course, have had anything to do with the precipitation of the attack. In another case, the spell began a few minutes after an increase in blood flow. In a patient with *petit mal*, a slight decrease in the rate of blood flow occurred after the onset of each seizure. From these observations, it appears that an increase rather than a decrease in blood flow is the rule. Nor can the spells be explained as a function of this increased flow, since the hypertension and muscular movements accompanying the episodes are adequate to account for

it. The theory that cerebral anemia precipitates epileptic convulsions, therefore, seems to be incorrect.

**Symptomatology.**—Using the Stanford revision of the Binet test, Joseph Fetterman and Margaret Barnes (Arch Neurol. and Psychiat 32:797 (Oct.) 1934) examined the *intelligence* of 105 epileptic patients attending a hospital dispensary. This group is considered intermediary between the deteriorated colony groups and the more or less superior private patient groups. The average I Q was 74. No relationship was found between duration and intelligence or between prolonged use of sedatives and I. Q. Nor did the patients show any deterioration intellectually when retested. It is, of course, possible that the epileptics in this study had already deteriorated from a previously high level before they came to the clinic, but during the period of observation the intelligence remained more or less stationary. The Binet test does not measure personality, and many of the features of so-called deterioration are really in the emotional rather than in the intellectual sphere. When the patients were grouped according to apparent etiology, the hysterical group showed the highest average I Q (81) and the organic group, the lowest (69). Six of the epileptics had I Q's in excess of 100, the intelligence quotient in one instance being 133.

In cases of untreated epilepsy, J. H. McLean (J Mental Sc 80 82 (Jan ) 1934) found that the *cholesterol content of the blood* is lowered during seizures. On the other hand, on both ketogenic and dehydration therapies, the cholesterol index rises. Its rise during ketosis is explained on a biochemical basis, while the increased cholesterol noted during dehydration is probably due to the mechanical concentration of all body chemicals because of water loss.

The commonly recognized "*epileptic personality*" consists of a desire to dominate and to resent interference, outbursts of temper, pugnacity, cruelty, sensitiveness, emotional instability and general sluggishness. Since these traits are so frequently associated with epilepsy, an hypothesis that they are intimately, perhaps organically, bound up with the disease, has developed. This, however, is probably not the case, according to E. M. Bridge (Arch Neurol and Psychiat 32 723 (Oct ) 1934). Most of these characteristics are explicable in terms of the effects of social pressure on the subject. Epileptics habitually encounter fear, prejudice and aversion. They are excluded from schools, from employment and from social contact. It is easy to understand how this form of social treatment would provoke a personality response of the so-called "epileptic" type. Instances of alteration in the epileptic's temperament with no physical improvement in the convulsive tendency, demonstrate that the disease cannot be a cause of the personality.

Some of the personality traits are definitely associated with the cycle of the seizures. Even in these cases, however, the personality may be normal in the interparoxysmal intervals, indicating that these characterologic changes cannot be structural. Of course, in the presence of gross brain damage (scars, tumors, cysts, etc ), the mental function is likely to be organically impaired, but these cases constitute only a small proportion of epileptics. The frequency of intellectual defect among epileptics has also been grossly overemphasized, part of this overemphasis being due to the use of scholastic aptitude ratings as intelligence

tests; the sluggishness which gives the patient the appearance of stupidity is often due to the medicine which is being administered. It is the author's ultimate conclusion that the so-called "epileptic personality" is not an entity which bears any specific causal relationship to the disease, but represents in large part the response of such patients to the problems and situations which the very nature of the disorder creates.

**Diagnosis.—Pitressin Test.**—Physicians often find it difficult to make a diagnosis of epilepsy because the patient fails to present any seizures during the period of the physician's observation. In order to induce a convulsion, so that the physician may have the opportunity of studying it and determining its nature, the pitressin-hydration technic may be used. This depends on the hypothesis that retained fluid can bring about a paroxysm. To perform this test, the following procedure is suggested by A. W. Jacobsen (New York State J. Med. 34: 506 (June) 1934): (1) Administer about 10 ounces of water by mouth every 2 hours. (2) Give hypodermically an injection of pitressin every 4 hours. The first dose should be 0.2 c.c. ( $3\frac{1}{2}$  minims), the second 0.3 c.c. (5 minims), the third 0.4 c.c. (7 minims), and the fourth and any subsequent doses, 0.5 c.c. (8 minims). Usually a seizure will occur within 48 hours on this régime. Fluid output should be measured and compared with fluid intake, so that a positive water balance (*i. e.*, more fluid taken in than excreted) will be attained. Another method of reaching the conclusion that a positive water balance has been attained is by weighing the patient very carefully every 4 hours. An increase in body weight of from 3 to 6 per cent over the weight at the beginning of the treatment usually represents sufficient fluid retention to induce a spell. When the spell occurs, all fluid and nourishment should be stopped, except for 1 c.c. (16 minims) of cream per pound of body weight every 4 hours. If the patient fails to have a seizure on this régime, the case is probably not one of epilepsy.

**Treatment.**—In many cases of epilepsy beginning during early childhood, particularly those periodically associated with eating or sleeping, an increased tendency towards vascular spasm depending on hormonal dysfunction, may play a major rôle. E. Lederer (Monatschr. f. Kinderh. 59: 359 (Mar. 21) 1934) has often succeeded in controlling spells by the administration of the circulatory **hormones obtained from striated muscle tissue** or from the **pancreas**. Some cases which resisted phenobarbital and bromides showed improvement on this régime. Lederer, accordingly, urges the use of these vasodilatory hormones, especially in instances in which the ordinary medical routine has proved ineffective. Among some of the newer methods of treating epilepsy, the author also lists **surgical procedures to relieve adhesions** (traumatic, inflammatory, etc.) **in the brain**. He points out that epilepsy is the product of 2 forces, *i. e.*, an irritant to the brain, and a reduced spasmodic threshold. The surgical procedures seek to relieve the disorder by removing the irritant, while the hormone treatment seeks to raise the spasmodic threshold.

The **hypertonic solution** employed by G. Villey-Desmeserets and J. Fr. Buvat (Paris méd. 2: 109 (Aug. 4) 1934) in the treatment of epilepsy consisted of (1) solution "A," composed of 2 Gm. (30 grams) of sodium chloride

dissolved in 20 c.c. (5 drams) of distilled water, and (2) solution "B" which contained 7 Gm. ( $1\frac{3}{4}$  drams) of sodium bromide and 1 Gm. (15 grains) of sodium chloride, dissolved in 20 c.c. (5 drams) of distilled water, and, in some cases, (3) solution "C" which consisted of 15 Gm. ( $3\frac{3}{4}$  drams) of magnesium sulphate dissolved in 150 c.c. (5 ounces) of boiled water.

Their program consisted of the intravenous injection of solution "A," followed in 2 or 3 days by the intravenous injection of solution "B"; 2 or 3 days later, solution "A" was again introduced intravenously, followed, in a few days by a second intravenous injection of "B." The solutions were thus alternated, 2 or 3 injections being given every week. Solution "C" was used only occasionally, and was given drop by drop by rectum. This treatment was given to 3 patients suffering from severe epilepsy, with favorable results in each case. The most seriously affected subject had about 130 spells a month. On this treatment, the frequency of the paroxysms was reduced to 4 or 5 a month.

A study by G. M. Griffiths (*J Neurol. and Psychopath.* 15 29 (July) 1934) of the calcium content of the blood in a series of 48 young epileptics showed no significant abnormality when the long-time average for each patient was calculated. However, certain associations between calcium values and the spells were found. In general, the pre-paroxysmal value was higher than the post-paroxysmal value, the blood calcium apparently falling during a seizure. During a succession of fits, high values were obtained, while after the termination of a series of such spells, the calcium findings were usually low. Two patients who died in status epilepticus showed particularly low calcium findings. The serum phosphorus was normal in most of the epileptics, nor were any significant alterations in calcium-phosphorus ratios noted. Griffiths suggests that treatment with large doses of calcium might have beneficial effects in epilepsy.

Physicians are often reluctant to use bromides in cases of epilepsy because of the reputation which this drug has for causing deterioration. H. A. Paskind (*J. A. M. A.* 103 100 (July 14) 1934) believes that such fears are unjustified. In a study of 304 epileptic patients, treated in various ways, adequate and inadequate, 6.5 per cent deteriorated. On the other hand, the analysis of 54 epileptics intensively treated with bromides over a period of years, shows that only 5.5 per cent of this group deteriorated. From this, it would appear that the deterioration was due to the epilepsy, not to the treatment. On the other hand, intolerably large doses of bromides will cause an attack of intoxication which may be mistaken for deterioration. However, these attacks are temporary, and symptoms will disappear on withdrawal of the drug. With proper adjustment of dosage, intoxication should not occur. Not only does bromide therapy cause no deterioration, but the patients who happen to deteriorate while on this régime are more often from the group treated inadequately than from the group treated intensively with bromides.

A series of 20 adult epileptics, aged 22 to 47 years, treated by the **ketogenic diet** is reported by John Notkin (*Arch Neurol. and Psychiat.* 31 787 (Apr) 1934). All of the patients showed some degree of mental deterioration, although they are reported as understanding the purpose of the diet and being willing to cooperate. The average duration of diet was 341 days. The urines were exam-

ined daily, and positive reactions for acetone were obtained 89.5 per cent. of the time.

Eighteen of the 20 patients had more spells when they were on the ketogenic diet than they had had before the institution of this régime. This could not be ascribed to sudden withdrawal of sedative medication, since some of these patients had not had any therapy before the diet was begun, and since the increase in the number of spells did not come early in the dietary régime. In fact, the number of spells between the withdrawal of the medication and the institution of the diet (a period of a week or two) was unchanged. Nor was there any relationship between the frequency or severity of the convulsions on one hand and the appearance or amount of acetone in the urine on the other.

Notkin concludes that ketogenic diet is not effective in controlling epileptic convulsions in deteriorated adult patients.

### ENCEPHALITIS.—EPIDEMIC ENCEPHALITIS.—*Pathology.*—

The 1933 epidemic of encephalitis in St. Louis differed from other epidemics of this disease in its seasonal incidence, occurring in the summer and early fall, instead of being the usual winter-spring type. Other points of difference were the absence of oculomotor paralysis, the intense restlessness, the absence of sequelæ, and the more favorable outlook. The present study by A. Weil (*Arch. Neurol. and Psychiat.* 31:1139 (June) 1934) is a histologic analysis of the brains of 8 patients who had had this form of encephalitis.

A mild, disseminated meningitis was found, most pronounced at the base of the midbrain. Foci of glial proliferation were found in the corona radiata, the cerebral peduncles, and particularly in the gray masses of the brain stem. Basically, the inflammatory reaction consisted of perivascular infiltration by small round cells and a few plasma cells and of the formation of isolated foci of proliferated glia. Small cocci, in chains or pairs, were demonstrated in every brain, representing possibly an agonal or postmortem infection. In 3 of the 8 brains, colonies of short-chain cocci were found within the glial foci and within thrombosed vessels.

In general, the histologic picture of this form of encephalitis was similar to that of other American epidemic forms.

Two unusual cases of encephalitis are presented by James Dawson, Jr. (*Ibid.* 31:685 (Apr.) 1934), in which the distinctive feature was the presence in the brain of intranuclear inclusions. These inclusions morphologically resemble those noted in herpes simplex in certain other virus diseases. They are not identical with the inclusions of herpes, however, nor are the two diseases produced by the same virus, as the biologic reactions to inoculation experiments demonstrate. The inclusions, however, do suggest that encephalitis is a virus-caused disease.

In the cases reported, the onset was sudden with no definite prodromal period. Fever was not high. Unconsciousness was present in one case, hallucinosis in the other. Involuntary, convulsive, jerking movements appeared in each instance. A parkinsonian syndrome subsequently developed in each patient. The spinal fluid cell count was 6 to 14, and sugar 58 in the first case, in the second, the

corresponding figures were 2 to 4 cells and 61 mg. of spinal fluid sugar. Both patients had skin lesions (herpes and eczema, respectively), and both became lethargic and died. At autopsy, glial scars (old) were found in both brains. Epivascular lymphocytic infiltration, acute necrosis of ganglion cells, capillary hemorrhages and edema, were found in each specimen. The acute changes were in the cortex, the chronic ones in the basal ganglia. The inclusion bodies were found in the acutely necrotic cells, suggesting that the virus was neurotropic. The type of encephalitis here described seems somewhat different from the usual form; the author designates these as cases of "inclusion encephalitis."

**Symptoms and Diagnosis.**—In the St. Louis epidemic of encephalitis during the summer of 1933, T. C. Hempelmann (J. A. M. A. 103:733 (Sept. 8) 1934) states that the onset was abrupt, with headache, fever and confusion. The course was stormy, usually lasting 2 or 3 weeks, with rapid recovery the rule. There is no evidence that this form of encephalitis resulted in any sequels. The disease was seen in 3 forms: the encephalitic from the onset, the mild or abortive, and the mixed form which looked like a general system infection for a few days, then gave evidence of neurologic involvement. In the latter form, the first phase of the disease was characterized by chills, weakness, nausea and headache. During the second phase, tremors, confusions, fever and stiff neck appeared.

The signs included rigidity of the neck and spine, absent abdominal reflexes, positive Kernig sign, inconstant tendon reflexes and occasional pathologic reflexes. Mentally, the picture was one of confusion and apathy, frequently with disorientation, and occasionally with excitement or aphasia. Blurring of vision occurred in 14 per cent of the cases and other ocular symptoms were even more rare. The leukocyte count usually fell between 12,000 and 20,000. The spinal fluid was clear, with a cell count of from 50 to 300, most of the cells being monocytes. Sugar was normal or slightly increased.

Other conditions from which this form of encephalitis must be differentiated include malaria, typhoid fever, poliomyelitis, tuberculous meningitis, and delirium tremens.

The acute (nonlethargic) encephalitis which appeared in St. Louis in the summer of 1933 marked the first epidemic of this disease in the United States. R. A. Kinsella and C. O. Brown (*Ibid.* 103:462 (Aug. 18) 1934) consider that the condition is clinically similar to the summer encephalitis of Japan and is to be distinguished from lethargic encephalitis of von Economo. The virus appears to enter through the upper nasal passages, reaching the brain directly. Onset is usually abrupt and the course febrile throughout. Stiff neck and vertical or frontal headache are almost invariably present. The mental state may be one of dullness or of mild delirium. Abnormal reflexes are frequently elicited at neurologic examination, but little of specific localizing value is usually found. Unlike the lethargic form, cranial nerve involvement is infrequent, although defects in pupillary responses to light and accommodation may occur. Painful spasms of muscle groups are common. The spinal fluid pressure shows little, if any increase. Globulin is usually present. In 86 per cent of the cases a tabetic gold curve was found, while in nearly all an increase in the spinal fluid cell count (between 50 and 100) was noted. The sugar level was slightly

increased and at times was as high as 100 mg. The average duration of illness, from onset to recovery was 10 days. The serious sequelæ of lethargic encephalitis have not developed, as yet, after attacks of the St. Louis form.

The disease must be *differentiated* from encephalitic phases of malaria and typhoid fever, which it may closely resemble. In making the differentiation between acute (St. Louis form) encephalitis and lethargic (von Economo) encephalitis, confidence may be placed in the "protective substance test." This consists in injecting a proportionate amount of serum from the patient simultaneously with a lethal dose of known infected material into the cranium of a white mouse; in lethargic encephalitis the serum contains protective substances adequate to afford to the mouse complete protection against the infection.

The general death rate in St. Louis was 20 per cent, but in the series reported by the authors, a mortality incidence of only 12 per cent. was found. Their *treatment* program consisted of: (1) **Lumbar puncture** to relieve headache and assist in making diagnosis; (2) **hypodermoclysis**; (3) administration of **liquid food**, by tube, if necessary; (4) **rest in a dark, noise-free room**, with few interruptions by visitors, doctors, or nurses, (5) **sedation**, using **morphine** if necessary.

**ENCEPHALITIS IN CHILDREN.—*Etiology.***—The possibility that the influenza organism may be the etiologic factor in encephalitis is strengthened by the 7 cases of encephalitis reported by W. B. Stewart (Am J M Sc 188: 522 (Oct) 1934), which occurred in children whose mothers had had influenza late in pregnancy. None of these 7 women appeared to have encephalitis, nor did any ever exhibit any of the postencephalitic sequelæ. Of the children born to these women, 4 had Parkinsonian syndromes, 1 had increasingly severe choreiform twitchings, 1 had a behavior disorder characteristic of the postencephalitic type of misbehavior, and the seventh showed lethargy and reverse Argyll Robertson pupils from birth. In all 7 cases, the postencephalitic symptoms existed at birth or developed shortly thereafter.

**ENCEPHALITIS AND INFLUENZA.**—In the early stages of influenza, a serous meningitic irritation may cause mild or vague nervous symptoms. However, a more definite involvement of the cerebral parenchyma may occur in the form of an influenzal meningitis or influenzal encephalitis. The latter begins with general nervous symptoms of a very varied sort, delirium or unconsciousness are rare initial findings. The peripheral nervous system may also be affected, so that an influenzal neuritis may occur. In influenzal encephalitis the foci may occur almost anywhere in the brain or brain-stem, and the subsequent neurologic findings depend on the site of the infectious focus. The location of such a focus in Broca's area, for example, would cause an aphasia and possibly an accompanying hemiplegia. *Treatment* should be directed against the influenza, and M. DeCrimis (Munchen med Wchnschr 81: 130 (Jan 26) 1934) recommends **convalescent serum**, **autohemotherapy**, **milk injections**, and, in some cases, intravenous injections of **methenamine**.

**ENCEPHALITIS LETHARGICA.—*Treatment.***—Three cases of encephalitis lethargica treated with minute doses of **x-rays** showed a lessening of the period of required hospitalization. S. A. Goldberg, C. F. Baker and

J. W. Hurff (Radiology 22:663 (June) 1934) believe that the efficacy of this form of treatment rests on the release of brain cells from pressure due to the inflammatory edema of the surrounding tissue. They suggest that x-ray therapy may be applied to cases of postencephalitic parkinsonism, although the extent of permanent damage makes them skeptical of the results in this form of encephalitis.

**SUMMER ENCEPHALITIS.**—The identity of the summer encephalitis of Japan and the acute lethargic encephalitis of von Economo has long been a subject of dispute. S. Naka, S. Kingo and K. Kuroiwa (Fukuoka-Ikwadaigaku-Zasshi 27:30 (Mar) 1934), however, are inclined to believe that these diseases are separate entities. Among the points of difference are: Japanese encephalitis occurs only during the summer, it attacks disproportionate numbers of the old and the very young, sleep disturbances are comparatively rare, cranial nerve involvement is infrequent.

The *symptoms* of Japanese encephalitis in order of their frequency are: headache, anorexia, debility, nausea, vomiting, somnolence and sleep disturbances. High fever with slow pulse occurs at the onset of the illness. A turning point is reached within the first few days, at which time the patient begins to convalesce, or enters a stage of apathy which is characterized by amnesia, slow thinking, perseveration, and various forms of aphasia. The mortality rate is 63 per cent.

**HEADACHE. — FRONTAL. — Etiology and Treatment.** — The syndrome of frontal headache due to *high intraocular pressure* is not generally recognized, according to R. L. Raymond (Brit M J 1:102 (Jan 20) 1934). The characteristic features of this entity are: frontal and temporal headache, usually severe, occurring in young persons in the third and fourth decades of life, pain increased by pressure on the eyeballs, when the pain is unilateral, pressure on the eyeball of the painful side produces an exacerbation of headache, while pressure on the other eyeball is negative. The measured eyeball tension is high, and in unilateral cases, higher on the painful side.

Four cases of this syndrome are presented. The patients were young males, the oldest 30, the youngest, 20. The headache was unilateral in each case, and the findings above described were elicited. Two of the patients had photophobia. All had normal vision, and except for the pressure, the ophthalmic findings were all normal. **Scopolamine** was instilled into the affected eye in each patient, and the results were uniformly good. One suffered a recurrence, the others were relieved of their pain in a month or two after the beginning of the treatment.

**INJURIES TO CENTRAL NERVOUS SYSTEM.—Pathology.**—The brains of 39 patients who had died following head injuries were subjected to histologic study. The findings were grouped by C. W. Rand and C. B. Courville (Arch. Neurol and Psychiat 31:527 (Mar) 1934) into 5 classes. (1) Minor cortical contusions—small, apical, dished-out lesions of the crests of the gyri, usually associated with small clots or milary hemorrhages, and some disintegration of the superficial layers of the cortex. The lesions were practically confined to gray matter. Many persons who survive head injuries have probably



sustained lesions of this type. (2) Moderate cortical contusions—extending into the white substance, involving some loss of cortical tissue and tearing of the overlying piaarachnoid. (3) Severe cortical lacerations and contusions—extensive bruising of the cortex and underlying white matter; hemorrhage from the subcortical vessels, destroying brain tissue. It is probable that this type of lesion exists in many cases of delayed death following severe head injury. (4) Intracerebral hemorrhage—gross subcortical hemorrhage which separates the cortex from the underlying nerve fibers. (5) Petechial hemorrhage—bleeding into the Virchow-Robin spaces, interrupting nerve fibers. The authors suggest that interruption of frontal lobe pathways by petechial hemorrhages may account for many of the so-called “neurotic” manifestations of the posttraumatic state.

Any of the lesions may interrupt nerve fibers. Since these fibers (within the brain) will not regenerate, functional loss resulting from such interruptions is permanent and the life of the cells from which the fibers arise is threatened. The interrupted nerve fibers undergo complete degeneration, especially in the distal segment.

The degenerative process begins within a few hours after the interruption of the fiber; fragmentation of the axis-cylinder begins within 6 hours, extensive changes are noted by the end of a 48-hour period. End-bulbs form at both proximal and distal ends of the interrupted segment. The bulbs at the distal end of the central segment maintain their identity for months or even years. The corresponding bulb on the proximal end of the distal segment soon disappears.

Residual clinical findings are so often observed following head trauma, even in cases not involving litigation, that N. W. Winkelman and J. L. Eckel (*Ibid* 31:956 (May) 1934) believe it is necessary to postulate some organic change within the cranium. In distinguishing mild from severe brain injuries, they are inclined to stress the importance of the period of unconsciousness. They suggest that the greater the duration of the unconsciousness, the greater the damage to the brain. They examined the brains of 7 persons who died several days or several weeks following injury. Gross hemorrhages with macerations of brain tissue were common in the rapidly fatal cases. In those who were apparently less severely injured, minute hemorrhages were more likely. When some obstruction to cerebral circulation developed, edema and ischemic focal necrosis were found; they suggest that these lesions may be important in explaining the symptoms occurring months or even years after the accident. Areas of generalized gliosis were also found, which tended to disappear slowly. Of particular interest and importance were the changes in the smaller blood-vessels. Small capillaries were often disproportionately prominent, probably the result of general anoxemia of the brain from the resultant edema. Subcortical petechiae were not uncommon. Small necrotic areas were found, even in the absence of free blood. Cerebellar softening, of the type seen in vascular occlusion, was found in one case.

Subarachnoid hemorrhage was the commonest of the gross lesions. Large and small hemorrhages within the brain substance were comparatively common. When edema set in, cerebral damage was increased. Many of the so-called “neurotic” symptoms are explained by these changes.

**Symptoms.**—I Strauss and N. Savitsky (*Ibid* 31:893 (May) 1934) state that the subjective complaints which follow head injury and are commonly ascribed to a traumatic neurosis are, in many cases, due to organic intracranial changes. The same syndrome (vertigo, headache, fatigue, etc.) is found all over the world, in both civil and litigated cases, with patients at varying intellectual and emotional levels, at all ages, with dissimilar personalities. In this very heterogeneous group, the only common factor is the head injury. It is much more reasonable to assume that the common symptoms spring from this obvious factor than to predicate a series of identical unconscious motivations. The pattern of the whole subjective syndrome bespeaks its organic nature.

Physicians examining patients who present various posttraumatic subjective complaints are cautioned to make an exhaustive neurologic examination. The organic lesions are often small and may give rise to objective signs which will escape the hasty examiner. Some of the findings commonly overlooked are: Difficulty in lateral conjugate gaze, slight tendency to fall to one side, changes in the corneal reflex, slight disorders in coordination, changes in muscle tonus, and slight postural defects. These findings may be of much significance, but few examiners take the trouble to determine their presence or absence. Often physicians do note trivial signs, but fail to record them because the findings are considered insignificant. Examiners should make it a rule to record every finding, regardless of their judgment about the ultimate interpretation of the sign.

The psychiatric interview should be a serious and thorough part of the examination. Intelligence, the sensorium, the volitional tendencies, the stability of the emotional processes, and the personality characteristics should be carefully noted. An impairment of a psychologic process, such as a mental defect, confusion, emotional instability or a defective memory, is as real and as important a disturbance as any of the objective findings in the organic neurologic sphere. Personality, achievement, memory and aptitude tests are of little value in most of these cases, because of the absence of data as to the pretraumatic status. A visual field determination should be made in all patients who complain of optic symptoms; the perimetry should include a determination of color fields. Persistent tubular contractions are usually hysterical; lesser degrees of cutting may be due to a variety of organic causes. Vestibular tests should be made accurately and the cochlear mechanism should be examined.

It is probable that many of the subjective symptoms are due to hydraulic changes in the central nervous system. For this reason, spinal fluid pressure determinations are often desirable. Special significance should be attached to very low manometric readings. Because of meningeal adhesions, the spinal fluid pressure may be normal in the presence of increased intracranial pressure. An increased protein content is indicative of meningeal or parenchymatous involvement. Encephalography is a valuable adjuvant in many cases. This procedure often indicates the organic basis of many complaints which otherwise baffle investigation.

The cerebral vasomotor mechanism plays an important rôle in concussion. Derangement of cerebral circulation appears to be responsible for many of the subjective complaints following concussion. Naturally, mental activity, physical

effort or emotional excitement will precipitate symptoms in the presence of an inefficient or irritable cerebral circulation.

There is no reason to assume that unconsciousness must accompany every case of concussion. Any blow severe enough to disrupt intracranial equilibrium constitutes a concussion. Of course, psychogenic features may be superimposed on an organic condition.

The authors conclude that the subjective posttraumatic symptoms are dependent on disturbances of intracranial equilibrium due to the blow on the head; that negative results on neurologic examination are no criteria of the presence, absence, or degree of damage to the brain; that significant intracranial injury may occur without loss of consciousness, and that psychogenic factors are likely to complicate, rather than to cause the clinical picture.

**Diagnosis and Treatment.**—The value of *encephalography* in patients with histories of head injury is stressed by A. Lippens and L. Dejardin (*Presse méd.* 42:455 (Mar. 21) 1934). The technic of injecting air intrathecally is described in detail, and the postural movements required are outlined. They recommend that the films be taken in 4 positions—right lateral, left lateral, prone, and supine. In certain cases of head injury an inequality in the sizes of the lateral ventricles is observed. In such cases, the ventricle on the traumatized side is likely to be larger. This usually indicates the part of the brain injured, regardless of the side of the skull apparently affected by the trauma. Stereoscopic films are recommended in the study of these encephalograms.

Seventy-five cases are presented. In many of them, the encephalogram was of great diagnostic aid. In one case it was possible to make a positive diagnosis 20 years after the original head injury. Under some circumstances direct injection of the ventricles (ventriculography) is performed.

In the management of a patient with head injury, Donald Munro (*New England J Med* 210:287 (Feb 8) 1934) states that first consideration must be given to the determination of the presence of *surgical shock*. A falling pulse pressure, a low temperature, a tachycardia, and a pale, moist skin require prompt treatment directed towards shock, and should discourage any other therapeutic procedures, and any meddlesome diagnostic procedures. Diagnosis of a *compound fracture of the vault* is made more readily and more accurately by palpation through the scalp wound than by x-ray. If *concussion* is the sole cerebral condition, no treatment is necessary. Gross brain damage usually takes the form of edema, contusions, or laceration. *Edema* is manifested by a short period of coma, altered tendon and abdominal reflexes, and sometimes convulsions or amnesia, with a clear spinal fluid under normal or very slightly increased pressure.

In *contusion*, the coma and amnesia are more prolonged, the headache more severe. Disorientation, abnormal reflexes, and confusion occur in varying degrees. Spinal fluid is yellow or pink, protein increased, and pressure is moderately elevated. In *laceration*, surgical shock is almost always present. Mental symptoms are likely to be pronounced unless coma is deep. Muscle flaccidity and sphincter incontinence are the rule. Temperature rises, the neck becomes stiff, the pupils wide, the pulse slow. Consciousness returns slowly and head-

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the symptoms follow the clinical pattern of the corresponding neurosis of non-traumatic type.

Among the characteristic symptoms of traumatic neuroses may be listed: weakness disproportionate to the objectively measured strength of the patient; numerous bizarre, hypochondriac complaints; occipital or vertical headache, usually a pressure sense rather than actual pain, and differing from organic headache in being continuous rather than intermittent; tremors, sweating, dilated pupils; anesthetics, paralyses, and disturbances in the special senses, usually nonanatomic in distribution and responsive to suggestion; and a peculiar emotional state.

The emotional state peculiar to the traumatic neurosis is a combination of fear, anxiety, suspicion and resentment. There is a tendency to explain all disabilities, regardless of their duration and of their obvious lack of relationship to the accident. An irresponsiveness to medication and therapy is usually noted.

It is futile, the authors state, to approach the posttraumatic neurosis from the anatomic or pathologic aspect; it must be studied from the psychologic standpoint. Such study usually reveals that even before the injury, the patient was neurotic or displayed certain personality inadequacies. The neurosis is in no sense caused by the accident; it is precipitated by it. The fact that even after litigation has been concluded, the symptoms may persist, is cited as evidence of a pretraumatic personality abnormality. Ultimately, the etiologic factors date from childhood, and the symptoms have their origin in these experiences and not in any organic cerebral changes. Of course, the process whereby the patient persuades himself of the severity and gravity of his complaints is a wholly unconscious one.

*Treatment* would require a reeducation of the individual in a new attitude towards life and its problems. Specifically, the authors suggest that, (1) the physician must not antagonize the patient by arguing with him or ridiculing him, (2) he must listen to the story, win the patient's confidence, and constitute himself his friend and ally, (3) payment, if any is due, should be made in a lump sum and not extended over a long period; (4) work should be provided as a diversion for the patient and as objective evidence of his own capacity, (5) some form of treatment, medical or physiotherapeutic, should be provided to afford the patient a reason for getting well without obliging him to ascribe his improvement to psychic factors.

**SPINAL CONCUSSION.**—Permanent organic changes may develop in the spinal cord following back injuries in which there is no direct pressure upon the cord, no gross hemorrhage into it, and no vertebral fractures, according to R. S. Baldwin (*Arch Neurol and Psychiat* 32:493 (Sept) 1934). Cases of this sort constitute true spinal concussion and must be distinguished both clinically and pathologically from hematomyelia. The changes which occur in the cord are most marked at the site of the injury, but may be scattered throughout the organ. Two cases are reported in which complete paraplegia, retention of urine, and marked sensory disturbances occurred. In neither case was there any fracture of a vertebra or other evidence of direct compression. The nerve fibers exhibited both primary and secondary degenerations, while in the

parenchyma, foci of softening were found. In many areas ganglion cells were distorted. Baldwin considers this picture the pathologic manifestation of concussion of the spinal cord.

**MENINGITIS.—*Diagnosis.***—No single *spinal fluid* factor is a reliable index to the existence or nature of a meningitis. While sugar determination is always valuable, it is, as J. Geldrich (*Deutsche med Wchnschr.* 60: 472 (Mar 30) 1934) points out, often difficult to measure accurately. He suggests that more attention be paid to the *lactic acid* value. More than 40 mg. of lactic acid per 100 c c of fluid is always suggestive of an infectious meningitis. The *Hopkins test* (sulphuric acid, copper sulphate, and thiophene) is recommended by Geldrich.

***Prognosis.***—Determination of the *chloride content* is stressed by L. O. Finkelstein and F. S. Merson (*Rev franç. de pediat* 10: 204 (Feb ) 1934). The normal figure is 720 to 740 mg per 100 c c. In *serous (lymphocytic) meningitis*, normal figures are found. In *meningococcic meningitis* the chloride content is reduced: the more severe the infection, the lower the chloride index. In *tuberculous meningitis*, this reduction in chlorides is even more noticeable. Finkelstein and Merson point out that chloride content may be used as an index of prognosis, a falling chloride value being an unfavorable, and a rising figure, a hopeful sign.

**CHRONIC MENINGITIS.—*Treatment.***—A case of chronic meningitis in a young man favorably influenced by **x-rays** is reported by H. Hippe and F. Lickint (*Klin Wchnschr.* 13: 1022 (July 14) 1934). The patient had severe spinal pain, low grade continuous fever, and poor nourishment. The area from the external occipital protuberance to the coccyx was subjected to x-ray therapy. This area was divided into 7 fields, and 20 per cent of a skin unit dose applied to each such field. (X-ray constants were as follows: Distance, 30 cm., strength, 6 ma., tension, 160,000 volts, filter aluminum and copper, 1 mm. and 0.5 mm., respectively.)

Two or three irradiations were administered a week. Seven treatments constituted a series, and one series was given during each calendar month for 3 months. This treatment reduced the pain, improved the nourishment and general tone, and made it possible for the patient to return to work.

Instances of the favorable effect of x-rays on the subacute forms of epidemic meningitis are enumerated. Reports of x-ray treatment in tuberculous meningitis are generally unfavorable. In some cases of serous meningitis this modality has produced good results. The authors particularly recommend it for the chronic forms of meningitis of all types.

**ACUTE LYMPHOCYTIC MENINGITIS.**—A form of meningitis which has been found by J. L. Abramson (*Arch Neurol and Psychiat* 31: 1235 (June) 1934) to be inadequately reported in this country, but carefully studied in Europe, is the "serous" or "benign" meningitis characterized by a spinal fluid lymphocytosis. The prodromal period lasts a week or two, during which time the patient may have a mild nose or throat infection. Onset is sudden, with headache, malaise, and vomiting. Fever, stiff neck, and the Kernig sign,

are likely to be present but mild. In adults, blurring of the discs is fairly common. Spinal fluid cytology shows hundreds, or even thousands, of cells, almost exclusively lymphocytes. Smears and cultures from both spinal fluid and blood will be persistently negative. The course of the illness is from 1 to 9 weeks, and the outcome almost always favorable. Consciousness is rarely disturbed, and sequelæ are unusual. The disease may be related to poliomyelitis or to encephalitis, as it has been reported during poliomyelitis epidemics, and the clinical courses of these two diseases are somewhat similar. In some instances, parkinsonism has developed in patients who had had attacks of serous meningitis, suggesting that this disorder may be another of the many forms of encephalitis.

Eight cases of serous meningitis (lymphocytic meningitis) are reported by the author. The age range was 19 to 38. Four of the patients were females. One patient had a positive Babinski, 2 had cranial nerve involvement, and 7 had both a Kernig sign and stiffness of the neck. Two of the patients had temperatures reaching as high as 104° F. (40° C.), but in 5 the temperature never exceeded 101° F. (38.3° C.). The number of cells found in the spinal fluid exceeded 1000 in 3 cases; and the proportion of lymphocytes varied between 98 and 100 per cent.

**INFLUENZAL MENINGITIS.**—Many of the deaths which occur in cases of meningitis in spite of vigorous treatment are probably due to infection with the influenza bacillus. Clinically, influenzal meningitis is indistinguishable from other forms of purulent meningeal infection, and the *diagnosis* must be based on spinal fluid findings, according to Benjamin Rittenberg (J. A. M. A. 102:1674 (May 19) 1934). Globulin and albumen in the fluid are likely to be increased, and sugar diminished or absent. The pathognomonic finding is the recognition of the Pfeiffer bacillus in the spinal fluid. The tube of fluid should be centrifuged immediately after the puncture, and a smear promptly made and stained. Because it takes several days to grow the bacilli on culture media, it is important to be able to recognize the organism from a smear of the centrifugate.

The *prognosis* is bad. Mortality rates are variously reported as ranging from 92 to 100 per cent. In the series presented by Josephine B. Neal, H. W. Jackson, and Emanuel Appelbaum (*Ibid.* 102:513 (Feb.) 1934) 107 out of 111 cases died, with a mortality rate of 96.5 per cent. Prior to this year only 32 cases with recovery had been reported in the literature. To this small number, 6 recoveries have been added in 1934; 1 by D. H. Duncan and C. H. Webb (J. Pediat. 4:216 (Feb.) 1934), 1 by Rittenberg, (*loc. cit.*) and 4 by Neal and her colleagues (*loc. cit.*)

**Spinal drainage** is emphasized as the essential *treatment* factor, both by Duncan and Webb (*loc. cit.*) and by Neal, Jackson and Appelbaum (*loc. cit.*). The latter workers are uncertain of the value of the **anti-influenza serum**. Rittenberg (*loc. cit.*), however, is inclined to ascribe success in treating this disorder to the prompt use of this serum. In his own case, 15 c.c. of anti-influenza serum mixed with 5 c.c. of fresh complement, were given every 8 hours for 6 doses, then every 12 hours for 6 doses, and then daily until recovery was assured. In the 35 cases reported since 1900 in which recovery had occurred, the serum was used 8 times; in all 35 instances, however, lumbar puncture was extensively

employed. Since no anti-influenza serum was used in most (77 per cent.) of these cases, while lumbar puncture was invariably performed, the statistics seem to support Neal's skepticism of the value of the specific serum. Rittenberg urges that complement be mixed with the serum, but Neal considers this of no value.

If the patient does not improve under serum therapy, Rittenberg suggests that another brand be employed, since the various biologic supply houses make up their sera from different strains of the Pfeiffer bacillus. Injection of the serum should be intrathecal, following spinal drainage; the intracarotid route, in Neal's opinion, is both futile and dangerous.

**MENINGOCOCCIC MENINGITIS.**—*Complication.*—*Obstructive hydrocephalus* is a rare but serious complication of meningococcic meningitis. Ordinary serum therapy by lumbar puncture is of little avail, and more radical measures are necessary. In the case reported by Arthur Antenucci and Seaton Sailer (J. A. M. A. 102:690 (Feb. 24) 1934), the patient had what appeared to be an ordinary case of meningococcic meningitis and was treated with **intrathecal (lumbar) injection of serum**. Four or 5 weeks after admission, she was stuporous, showed choked disc and unequal pupils. A **ventricular puncture** was done under local anesthesia. Two centimeters to the right and  $6\frac{1}{2}$  anterior to the occipital protuberance (external), the skull was opened and a needle plunged into the ventricle. Fifty-five c.c. of fluid were removed and 15 c.c. of antimeningococcus serum instilled. The temperature dropped and the condition improved immediately after this procedure, but within 4 weeks stupor reappeared and twitchings were noted. The ventricular puncture and drainage were repeated but no serum was given. A slow but uneventful recovery followed.

*Treatment.*—The beneficial results of **spinal insufflation of air** in cases of cerebrospinal fever are probably due to the fact that the warmed, rising air forces out infected fluid. Secondly, good effect is produced by breaking up the adhesions, thus preventing the development of hydrocephalus. Ivan Matovetsky (Klin. med. 12:1011 (May 26) 1934) reports the results of this form of treatment in 15 cases. Eleven of these recovered and exhibited no pathologic sequels. Of the 4 who died, 1 already had had a bacteremia before the institution of treatment.

The technic, as outlined by the author, consists in lumbar puncture with removal of 20 to 30 c.c. of fluid (depending on the age of the patient); the needle is retained in place, and a sterile syringe is attached. The syringe is then compressed, forcing in from 5 to 15 c.c. of air. The syringe is then detached, permitting more fluid to trickle out, and a few minutes later another air injection is given. This procedure is repeated from 3 to 7 times a week depending on the severity of the case, and is continued until the fluid is clear.

Immediately after the treatment, headache and backache may become aggravated. Within 2 or 3 hours, however, these symptoms abate, the temperature falls, and the clinical state improves.

**PNEUMOCOCCIC MENINGITIS.**—Pneumococcic meningitis is almost invariably fatal; the case reported by Caroline Bedell (J. A. M. A. 102:820



(Mar. 17) 1934), however, was one in which recovery followed radical operative cisternal puncture and cisternal-lumbar drainage.

The patient had severe right-sided supraorbital headache, high fever, stiff neck, edematous eyelid, positive Kernig sign, stupor, and hyperemia of the optic discs. Leukocyte count was 20,000, with the polymorphonuclears constituting 88 per cent. Spinal fluid was cloudy, but unflaked. Cytology showed 8000 white blood cells, mostly polymorphonuclears. Smear showed Gram-positive diplococci, and a pure culture of pneumococcus, type IV, was obtained.

*Treatment* consisted of combined **spinal and cisternal drainage**. A midline incision was made over the lower part of the occiput. A small opening was rongeuured in the bone, about 100 c.c. of fluid aspirated from the cisterna and a No. 14 soft rubber catheter inserted and sutured with silk to the dura. The dura was left open above and below the tube. By this method 200 c.c. of fluid was drained from the cisterna. Many holes at the cisternal end of the tube permitted free drainage through the catheter. Lumbar puncture was performed every 24 hours for 13 days. **Warm, physiologic sodium chloride solution** was instilled by gravity into the cisterna through the catheter and removed by the same route to wash out flakes of exudate. Then 50 c.c. of the same solution, sterile, was instilled into the cisterna and permitted to escape through the lumbar needle.

To reduce the volume of the brain by dehydration, 100 c.c. of 50 per cent **dextrose** were given intravenously. Two hours later, **fluids were forced**.

Supplementary therapeutic measures included **paraldehyde** by rectum, **morphine** hypodermically, **restraint**, **liquid diet**, **blood transfusion**, and **saline infusions**.

Following the insertions of the cisternal drainage catheter, the temperature fell from 106° to 102° F (41.1° to 38.9° C). Clinical improvement was slow for the first 10 days, rapid, thereafter. After the saline irrigations were started, growth of the pneumococci was no longer obtained. The patient was discharged, recovered, 3 weeks after admission.

It is probable that only early cases of pneumococcic meningitis would respond so favorably to this form of therapy. In a disease as fulminating as this, it is only a matter of hours before the thickness of the meningeal exudate and the formation of adhesions would destroy the value of this technic. Stress is laid on the fact that 200 c.c. of fluid escaped from the cisternal tube daily, far exceeding the amount usually obtained in cases of purulent meningitis drained solely by repeated spinal taps.

**RADICULAR MENINGITIS.**—Meningitis may take a radicular form, affecting chiefly the spinal nerve roots, according to V. Christiansen (Hospitals-tid 77:749 (June 26) 1934). The onset is acute and the symptoms include paresthesias, paraplegias or monoplegias, and sensory defects. Urinary incontinence or pain on micturition may be noted. Paralyzes occurring in the course of this disease are usually flaccid, but spastic palsies, particularly of the lower extremities, may occur. Care must be exercised to distinguish radicular meningitis from cerebrospinal syphilis, and because of the clinical similarity between the two conditions, a spinal serology is required. Peripheral neuritis and spinal compres-

sion from tumors or other sources may also cause confusion in differential diagnosis. In radicular meningitis, recovery is the rule

**TUBERCULOUS MENINGITIS.**—*Diagnosis.*—In a series of 12 proved cases of tuberculous meningitis, M. B. Rosenblatt (Am Rev. Tuberc 29. 688 (June) 1934) found the *tryptophan test* was positive in the spinal fluid in every instance. Doubtful positive reactions were obtained in some cases of increased protein, as in hemorrhagic, xanthochromic, or purulent fluid. Even in these cases, however, the color reaction was different from that obtained in tuberculous meningitis. The author suggests the use of the tryptophan test as a routine procedure in the examination of the cerebrospinal fluid

**MIGRAINE.**—*Etiology.*—Migraine may be considered a syndrome of allergic origin according to A. F. Andresen (Am J. Digest. Dis and Nutrition 1. 14 (Mar.) 1934). Even in those cases where focal infection plays an obvious rôle, an allergic mechanism is at work, since in those patients, sensitization to the bacterial proteins at the infected locus is a factor. Menstrual migraine represents an allergy to the ovarian hormone, while other endocrine dysfunctions indicate that the patient has become sensitive to his own internal secretions. Sudden transient edema of certain tissues is a common concomitant of allergic attacks, and in migraine it is probable that the brain and meninges become the seat of this transient edema.

*Diagnosis* is based on a family or personal history of allergic manifestations, on the characteristic attack, on the determination of the allergic factor and the response to its removal, and in some cases on an eosinophilia. To determine the specific allergic factor, skin tests, actual trial with various foodstuffs, and analyses of attacks may be necessary. The ultimate determinant is the demonstration that the paroxysm will not occur unless certain foods are included in the diet.

*Prophylaxis* consists of avoiding the offending food. If one of the very common foods, such as egg, wheat, or potato, is the factor, desensitization by gradual increasing doses or by the use of the specific food peptone is indicated.

*Treatment* of an attack consists of administration of **epinephrine** (1:1000 solution) in a dosage of from 0.6 to 1 c.c. (10 to 16 minims), intramuscularly or sublingually. **Ephedrine** may be given orally for prolonged but slower effect. The vomiting may be relieved by **gastric lavage**. Catharsis by means of **castor oil** is usually a useful procedure, not only to remove the offending food from the intestinal tract, but also, by virtue of the ricinoleic acid contained in the oil, as a detoxicating agent. **Pituitary extract** often gives good results. **Rest** and the application of **cold** or of **heat to the head** will afford relief. Coal-tar sedatives should be used cautiously. The basic treatment, however, consists in the **removal or the neutralization of the offending protein**, usually a food stuff.

*Relationship of Migraine, Epilepsy and Some Other Neuropsychiatric Disorders.*—Analyzing the family histories of 3300 private neurologic patients, H. A. Paskind (Arch Neurol and Psychiat 32. 45 (July) 1934) finds that migraine is reported in the family history of 35 per cent of the epileptics, and

in only 14 per cent. of the families of a group of controls (normal persons). However, a migraine history is also found in almost 50 per cent. of the families of the patients with constitutional inferiority, in 37 per cent. of those with tic, and in 38 per cent. of those with trigeminal neuralgia. It would appear, therefore, that there is a closer relationship between tic and migraine, or between trigeminal neuralgia and migraine, than between epilepsy and migraine. In the group of dementia precox and manic-depressive patients, a migrainous family history was reported in 32 and 34 per cent., respectively, an incidence of proportions similar to the family histories of epileptics. Of a group of epileptics, only 8 per cent. had migraine, whereas 10 per cent. of the manic-depressive patients had this disorder.

Paskind concludes that there is no special relationship between migraine and epilepsy, and that migraine occurs as evidence of a familial neuropathic trend in many other neuropsychiatric conditions.

**Pathogenesis.**—The headache, visual disturbances, and vomiting associated with migraine are also found in certain forms of uremia. Eugene Foldes (Am. J. Digest. Dis. and Nutrition 1: 359 (Aug.) 1934) believes that the underlying pathogenic factor in the latter condition is increased intracranial pressure, due to retention of fluids. On this basis, he accounts for the association between migrainous paroxysms and changes in the weather: when the barometric pressure falls, fluids within the body are retained, thus increasing intracranial pressure. The common cold, like most infectious diseases, is also associated with fluid retention, and hence with exacerbations of migrainous headache. (The relationship between migraine and epilepsy, on the basis of the analogous periodicity of these two paroxysmal disorders, has often been mentioned; in this connection the explanation of epileptic spells in terms of fluid accumulation may be recalled.)

Foldes suggests, therefore, that elimination of fluid and the prevention of excessive intratissual fluid accumulations be the keystones of the *therapy* in the management of a case of migraine. A diet should be prescribed which will stimulate the elimination of fluid and discourage fluid reaccumulation. Good results are reported on this so-called **antiretention diet**.

**Treatment.**—The present-day treatment of migraine is described by W. C. Alvarez (Proc. Staff Meet. Mayo Clin 9: 22 (Jan.) 1934) as follows. During an attack of migraine the patient should go to **bed in a darkened room**; a **laxative** taken at this time will often give relief. A hypnotic, such as **phenobarbital** or **amytal**, should be given in order to induce sleep. Usually, on awakening the attack will be gone. If *vomiting* is a persistent symptom, rectal injections of **potassium bromide** (20 to 40 grams—1.3 to 2.6 Gm.) and **chloral hydrate** (10 to 20 grams—0.65 to 1.3 Gm.) may be given. **Sodium amytal** may be administered hypodermically if oral medication cannot be retained. During an attack the following are worthy of trial: **antuitrin**, 1 cc (16 minims), hypodermically; **ergotamine tartrate (gynergen)**, 0.5 mg ( $\frac{1}{120}$  grain) intramuscularly; **epinephrine** (1:1000 solution)—10 to 20 minims (0.6 to 1.2 cc), hypodermically; **sodium thiosulphate**, 1 Gm (15 grains), **nitroglycerin**, hypodermically,  $\frac{1}{100}$  grain (0.6 mg.).

The prolonged treatment may consist of any of the following preparations: **calcium gluconate**, tablets of 10 or 15 Gm. (15 to 23 grains), 1 or 2 tablets 3 times a day, **chondroitin-sulphuric acid**, 3 Gm (45 grains) per day, **peptone**, 5 per cent solution intravenously, 0.5 cc (8 minims), increasing to 20 cc ( $\frac{1}{2}$  dram), 2 injections a week; **ergotamine tartrate**, 0.5 mg. ( $\frac{1}{120}$  grain) twice a day intramuscularly, **typhoid vaccine; aolan; theelin** hypodermically in 1 or 2 cc. (16 or 32 minims) doses, on alternate days, **progynon** twice a day, for 10 days each month, **tuberculin**.

Patients with migraine often complain of tetany-like symptoms, such as tingling, hyperpnea, and muscular cramps. In many of these cases a low blood calcium is found. G. F. Norman (J. A. M. A 102:529 (Feb 17) 1934) believes that the migrainous tendency is physiologically akin to the convulsive tendency and that it is held in check by the maintenance of a proper calcium balance. He presents a series of 70 patients with migraine who improved under **viosterol** or **parathyroid therapy**. The dosage and effects of this therapy are illustrated by the following protocols:

1 Weekly attacks of migraine, **viosterol**, 3 drops, 3 times a day, complete relief as long as patient remained on medication.

2 Migraine both in patient and in family history, no relief from other forms of therapy, blood calcium 7.5 mg per 100 cc of blood (normal is 11); **viosterol**, 4 drops, 3 times a day, headaches absent while patient remained on viosterol, returned when medicine was abandoned.

3 Migraine with blood calcium of 6.5–10 units of **parathyroid extract** by mouth supplemented by **viosterol**, 10 drops, t.i.d. No headache for months thereafter, blood calcium rising to 12. Medication discontinued, and headaches returned 2 weeks later, blood calcium dropping to 8.6. Viosterol resumed and attacks ceased.

4 Migraine with tingling and muscular cramps, positive Chvostek and Trousseau phenomena. Blood calcium 7.6. Received **parathyroid extract**, 20 units, with dramatic relief. **Viosterol**, 10 drops, t.i.d. and no headache for a month, when dosage was dropped to 7 drops, and headaches promptly reappeared. Ten drop dosage restored and supplemented by parathyroid, 10 units daily, with complete relief.

5 Irregular respiration, muscle cramps, and migraine. Positive Chvostek phenomena. Blood calcium 6.5. Immediate improvement on **viosterol**, calcium rising to 13.3. Medication discontinued and attacks recurred. Relieved by resumption of viosterol, 15 drops, t.i.d.

6 Cramping of muscles, parasthesias of extremities, blood calcium of 8.8. Relieved by **viosterol**, 3 drops, t.i.d., calcium rising to 9.6. Symptoms recurred on discontinuance of medication.

From these instances, it would appear that the symptoms of migraine may be inhibited by proper **calcium regulation**. When blood calcium falls below 9 mg per 100 cc of blood in cases of migraine, viosterol and parathyroid therapy offer promise of relief.

W. G. Lennox (New England J. Med. 210:1061 (May 17) 1934) reports prompt relief in 40 out of 45 sufferers from migraine by the administration of

**ergotamine tartrate (gynergen).** The relief persisted beyond the action period of the drug. Some untoward effects occurred, including nausea, vomiting, dyspnea and bradycardia. The preparation should be used cautiously in patients with vascular disease, and not at all in pregnant women. It may be administered intravenously, subcutaneously, or orally. The former is the most effective method, and should be given in this manner in a 0.25 mg. ( $\frac{1}{240}$  grain) dosage. The subcutaneous dose is 0.5 mg. ( $\frac{1}{20}$  grain), although only half this amount should be used at first in order to test the patient's tolerance. For oral administration 1 mg. ( $\frac{1}{65}$  grain) should be given at a time. The dosages may be combined (2 routes of administration being used at once, in *pro rata* fractional doses), and the medication may be repeated after an interval of 2 or 3 hours. Relief should be experienced within  $\frac{1}{2}$  hour after intravenous use, and within 2 or 3 hours after oral administration. When given subcutaneously, the drug relieves the headache within an hour or two. Whether ergotamine tartrate produces this effect by direct inhibition of the sensory nerve ending or indirectly by paralyzing motor sympathetics and relieving vascular spasm, has not been established.

It has also been found by A. H. Logan and E. V. Allen (Proc. Staff Meet Mayo Clin. 9:585, 1934) that the headaches of migraine are usually relieved by the administration of **ergotamine tartrate (gynergen)**; this preparation, however, is not a cure or even a specific remedy. The first dose of ergotamine tartrate should be 0.25 mg. ( $\frac{1}{240}$  grain) (which is 0.5 c.c. of the solution). A second dose, twice the strength of the initial one, may be administered in 3 hours if the patient has not been relieved. If the headache has diminished but is still annoying, the second dose should be the same strength as the first. The ergotamine tartrate may be given intravenously or hypodermically: by the subcutaneous route the dosages indicated should be used, lesser amounts are required if the more effective intravenous technic is employed. If there is no nausea, from 1 to 3 mg. ( $\frac{1}{65}$  to  $\frac{1}{20}$  grain) may be given by mouth in divided doses. If the patient is pregnant, ergotamine tartrate should not be used, and in the presence of hypertension it should be administered very cautiously.

In an analysis of 71 attacks of headache in 9 patients, the authors found that this preparation relieved 69 of the migrainous paroxysms.

**MULTIPLE SCLEROSIS.—Etiology.**—In a typical case of multiple sclerosis, W. Cone, C. Russel and R. W. Harwood (Arch. Neurol. and Psychiat. 31:236 (Feb.) 1934) found lead in the spinal cord at autopsy. Six patients with multiple sclerosis showed lead in the stools, urine, and spinal fluid. It is known that lead has a demyelinating action on the peripheral nerves of man and higher animals, and demyelination is the primary pathologic process underlying multiple sclerosis. On the other hand, the demyelinating action of lead is definitely known only in so far as it affects the peripheral nerves. While degenerated areas in the spinal cord have been occasionally reported in lead poisoning, the characteristic demyelination of the cord has not been clearly associated with lead poisoning. The authors suggest that this evidence tends strongly to incriminate lead as at least a potential causative factor in some cases of multiple sclerosis.

**Pathology.**—Multiple sclerosis is usually considered an upper motor neurone disease, with spasticity as its characteristic sign. Nevertheless, cases of flaccidity accompanying this entity are occasionally seen. In a series of 20 cases of multiple sclerosis which came to autopsy, C. Davison, S. P. Goodhart and J. Lander (*Ibid* p. 270) found atrophy of one or more muscle groups in 12 subjects. In 11 of these 12 cases, the small muscles of the hand were involved in the amyotrophy. The tongue, shoulder muscles, biceps, sternomastoids, and extremities were implicated in various degrees in many of the cases. Mental changes and sphincter disturbances were noted clinically in 4 of the 12 cases of this group.

The pathologic basis for the amyotrophy was invasion of the anterior horns by the sclerotic plaques. The nerve cells were involved in primary changes for the most part, although degeneration secondary to destruction of the axones also played a rôle in the amyotrophy.

**Treatment.**—In the treatment of 8 cases of multiple sclerosis by Ludwig Horn (Wien. klin. Wchnschr 47:231 (Feb. 23) 1934) with **colloidal silver**, good results, including prolonged remissions, were obtained. The régime consists of a series of 3 injections, and from 8 to 12 of each series must be given. The program consists of the following schedule:

**First Day**—On an empty stomach, at 8 A. M., a teaspoonful of **bicarbonate of soda** by mouth. At 9 A. M., 5 c.c. ( $1\frac{1}{4}$  dram) of an electrolyzed **colloidal silver** preparation, by injection. Breakfast at 10 A. M. At 11 A. M., an intravenous injection of 33 per cent **dextrose** (10 c.c.— $2\frac{1}{2}$  drams). In the evening another teaspoonful of **sodium bicarbonate**.

**Second Day**—**Bicarbonate of soda** administered orally as on first day, morning and evening. On an empty stomach, an intravenous injection of 500 mg. ( $7\frac{1}{2}$  grains) of **sodium thiosulphate** dissolved in 10 c.c. ( $2\frac{1}{2}$  drams) of water.

No injections are given for 4 or 5 days, then a second series is administered. In each series, the second day treatment is the same, the dosage of the thiosulphate remaining unchanged during the whole course. In each series, however, the dose of the silver and the dextrose are increased. The second dose of the silver is 6 c.c. ( $1\frac{1}{2}$  drams), the third is 7 c.c. ( $1\frac{3}{4}$  drams), etc., until the eighth dose, which is 12 c.c. (3 drams). The dextrose solution is also increased by 1 c.c. (16 minims) a day.

Patients refractory to other forms of therapy have shown improvement on this régime.

On the theory that **lecithin** neutralizes the lipolytic substance present in the spinal fluid, M. H. Weinberg (J. Nerv. and Ment. Dis. 79:264 (Mar.) 1934) used this preparation in the treatment of 12 cases of multiple sclerosis. The lecithin is administered intraspinally, and **quinine hydrochloride** is given orally. **Codliver oil** should also be administered over long periods of time during the course of the lecithin therapy. Some improvement was noted in 9 of the 12 cases, and the author is inclined to evaluate the results as sufficiently good to warrant further study and continued use of the lecithin.

C. A. Neymann and S. L. Osborne (*Ibid* 79:423 (Apr.) 1934) treated 25 patients suffering from multiple sclerosis by **electropyrexia**. Diathermy, radio-

thermy, and the electric blanket were used. Of these patients, 10 (40 per cent.) showed some improvement, and 11 (44 per cent.) showed marked improvement. In the remaining 4 patients (16 per cent.) no improvement was observed. In no case, however, did improvement continue for long after the electropyrrexia was discontinued. Of the 4 unimproved patients, 1 died, probably as a result of the treatment. Another in this series of 4 unimproved cases died of an intercurrent disorder. Of the 21 improved cases, only 1 returned to the institution shortly after treatment with an exacerbation. The authors are skeptical of the ultimate success of this therapy, but believe it has some palliative value.

**MYASTHENIA GRAVIS.—Treatment.**—It is important that patients with this disease have adequate **rest**. The amount of rest depends to some degree on the individual case. **Food** is of prime importance. The difficulty in chewing and swallowing makes it necessary for the patient to have a soft, easily masticated, and yet highly nutritious type of food, which contains all necessary food elements. It is well to teach the patient to chew slowly. It may be necessary in the more severe cases to give nourishment by means of nasal tube, but the seriousness of possible complications of this procedure must be kept in mind. All forms of exercise including physical therapy and electrical treatments are contraindicated. Tonic medication has been most commonly employed, particularly **arsenic**, **phosphorus** and the **elixir iron, quinine and strychnine**. There are numerous reports in literature of beneficial results from treatment with large doses of strychnine, even as high as 2 or 3 grains (0.13 to 0.2 Gm.) 3 times daily. This dosage, however, must be arrived at by giving smaller dosages at first and gradually increasing until tolerance is reached. The injection of strychnine hypodermically is advocated by some, the dosage being as high as  $\frac{1}{10}$  grain (0.006 Gm.) 3 times per day. Calcium in the form of **di-calcium phosphate** has been of some value. Endocrine therapy has been advocated by many, especially **adrenalin** and the **cortical extract of the adrenals**. Some good results have been reported, but the results in most cases are rather disappointing. In some cases of myasthenia gravis the x-rays have demonstrated enlargement of the thymus, according to M. N. Zajewloschin (Ztschr. f. d. ges. Neurol. u. Psychiat. 148: 28 (Oct.) 1933). In these cases **x-ray therapy** of the thymus gland may be of value, according to L. Stone and M. M. Abeles (J. Nerv. and Ment. Dis. 80: 285 (Sept.) 1934), K. Briegleb (Med. Klin. 30: 305 (Mar. 2) 1934) and W. Gros (München med. Wchnschr. 81: 526 (Apr. 6) 1934), and appears to be a particularly successful type of therapy in selected cases. **Glycine** has also been used in doses of as much as 15 Gm. ( $3\frac{3}{4}$  drams) 3 times a day, and more recently the use of a combination of **glycine** and **ephedrine** has been reported by D. McAlpine (Lancet 1: 180 (Jan. 27) 1934) and W. M. Boothby (Arch. Int. Med. 53: 39 (Jan.) 1934). At the present time, the advocated dosage being ephedrine,  $\frac{3}{4}$  gram (0.024 Gm.), twice a day with **glycine**, 15 Gms. ( $3\frac{3}{4}$  grains), twice a day. Particular care should be taken to protect the patient against the development of any infection, or any situation in which muscular overactivity may occur and, above all, the patient should be impressed with the importance of **rest**.

Another endocrine treatment which has been advised by A. Slauck (Verhandl. d. deutsch. Gesellsch. f. inn. Med. Kong. 45:175, 1933) is that of the male sexual hormone, the one particularly advocated being **proviron**. It is said to have some influence on the creatin-creatinine metabolism, and the results in the use of this therapy were gratifying in all cases.

**MYOPATHIES.—Treatment.**—Older forms of treatment for all forms of myopathies have been of little value. A good many cases have shown some temporary improvement on treatment in the form of **calcium lactate**, especially if given with **parathyroid extract** and in the use of other certain hormones. **Pituitary extract** has been advised but it appears to be of little real value. The subcutaneous injection of  $\frac{1}{5}$  to  $\frac{3}{10}$  c.c. (0.013 to 0.019 minims) of 1 per cent. **adrenalin solution** and  $\frac{1}{10}$  to  $\frac{1}{5}$  c.c. (0.0065 to 0.013 minims) of 1 per cent. **pilocarpine hydrochloride solution** daily has given in some cases good results.

In view of the gland disturbances in the creatin-creatinine metabolism, considerable work has been done by A. Slauck (Verhandl. d. deutsch. Gesellsch. f. inn. Med. Kong. 45:175, 1933) on the use of amino-acids in the treatment of muscular dystrophies. It has been noted by S. Kostakow and A. Slauck (Deutsches Arch. f. klin. Med. 175:25, 1933) that there is an increase of creatinuria under the use of **glycocoll** or **glycine**. Other amino-acids such as alanin, histidine, cystin, arginin and glutamic acid have no effect on the creatinuria, according to W. Linneweh and F. Linneweh (*Ibid.* 176:526, 1934) and S. Kostakow and A. Slauck (*Ibid.* 175:302, 1933). The increase in creatinuria after glycocoll therapy has been regarded as evidence of a synthetic building of creatin, and the literature contains a gradually increasing number of reports of improvement following the use of this drug in the treatment of myopathies (S. Kostakow (*Ibid.* 176:467, 1934)). It appears to have more definite action in those cases of pseudohypertrophic muscular dystrophy. The drug is given in 5 to 15 Gm. ( $1\frac{1}{4}$  to  $3\frac{3}{4}$  dram) doses by mouth 3 times a day. The deformities which result from this condition, of course, should be palliatively treated by **orthopedic procedure**.

**NEURALGIA, TRIGEMINAL.—Treatment.**—T. Fracassi and F. L. Marelli (Rev. méd. del Rosario 24:743 (Aug.) 1934) treat essential trigeminal neuralgia by **electroneurolysis** with the following technique. The patient lies on his back on a flat table with the head in such a position that the involved nerve forms the continuation of a vertical line with the needle introduced vertically. This position of the nerve in relation to that of the needle is obtained by the inclination or by the elevation of the patient's head without changing the position of his body and is controlled by the position of the foramen ovale and the foramen rotundum. To approach the inferior and superior alveolar nerves, the patient's head is inclined in the first case and raised in the second case  $15^\circ$  from a line horizontal to the axis of his body. The needle used is one of those commonly used for intramuscular injections, not exceeding 4 or 5 cm. in length. A fine insulated copper wire, which can easily pass through the eye of the needle, previously disinfected with alcohol, is used as a mandrin. The layer of insulating thread of the mandrin is removed at one end 3 or 5 cm., and a knot made in the



mandrin as a mark to indicate the length which should be introduced in order to have its point pass the point of the needle. The other end of the wire is then connected with a galvanic current. A painful sensation of the patient, exteriorized by an involuntary gesticulation, indicates that the point of the mandrin is in contact with the involved nerve. The current is then stopped in order to perform the anesthetization of the nerve by infiltration of 1 c.c. of a 2 per cent. solution of **procaine hydrochloride-epinephrine**. Four or 5 minutes later the isolated mandrin is introduced down to the mark previously made on it. The other end of the wire is then connected to a galvanic current and this current is permitted to pass in a slow and progressive form until 5 ma. has been given during 3 or 5 minutes at each pole. The positive pole should be applied before the negative one, because the former adheres to the nerve and it is detached from it only by the passage of a negative current. Because of the fineness of the mandrin, the galvanic current does not destroy the tissues of the nerve during the first application. A second application, given 3 or 4 days later with the same technic, results in the destruction of a new zone of the nerve and the complete disappearance of the pain. In the authors' cases the pain has not reappeared up to the present (6 months after the treatment). They advise resorting to alcoholization of the nerve with 2 or 3 per cent. **phenolated alcohol** in cases in which the galvanization is impracticable. Phenolated alcohol is more efficient than absolute alcohol in these cases.

K. G. McKenzie (Canad. M. A. J. 29:492 (Nov.) 1933) points out that **partial section**, by the temporal route, is a much more satisfactory procedure than complete section in trigeminal neuralgia. This includes the fairly common type of patient in whom the pain commences in the second and third division and spreads up through the eye and forehead. In these patients the main trigger spots are in the second and third division, and partial section is usually indicated, even though a subsequent operation may occasionally be necessary. Complete section is condemned because of the number of severe eye complications. It is definitely indicated only in the comparatively few patients in whom the pain commences in the first division. Partial section by the temporal route is such a satisfactory, safe and simple procedure that the cerebellar approach advocated by Dandy has been adopted only occasionally. It is especially indicated when it is considered necessary to cut both the glossopharyngeal and trigeminal nerves and in patients in whom the presence of a small angle tumor is suspected. In 2 patients on whom partial section was performed after the manner described by Dandy, the sensory loss was identical with that usually found after partial section by the temporal route; these observations are at variance with the views of Dandy and Davis, the latter feeling that a partial section as described should cause the greatest sensory loss in the first division area, whereas Dandy states that there is no sensory loss.

**OCCUPATIONAL DISORDERS (NEUROLOGIC).—CHRONIC MANGANESE POISONING.**—The syndrome of chronic manganese poisoning consists of languor, masked facies, monotonous voice, muscular twitchings and cramps in a patient who has been exposed to manganese dust for at

least 3 months. These patients even when removed from the hazard display little improvement and live for years as healthy but more or less helpless invalids. M. Canavan, S. Cobb and C. Drinker (Arch. Neurol. and Psychiat. 32: 501 (Sept.) 1934) cite 2 cases of manganese poisoning with parkinsonian syndromes. The work of Lewy and Tiefenbach in producing changes in the corpora striata by the administration of manganese salts is recalled.

The case of chronic manganese poisoning is reported in a man who worked for 4 years in a mill where manganese-containing fractions were separated from other ores. In 1918, this patient suffered from difficulty in walking, clumsiness, awkwardness, nocturnal muscular cramps, tendency to fall asleep while at work, propulsion, and a stolid, mask-like face. Reexamined periodically between 1918 and 1928, he showed no regression and no improvement. He died in 1931 of cardiorenal disease.

Autopsy showed some atrophy of the left cortex and indistinctness in the basal ganglia. Examination of the striate bodies and thalamus showed atrophy. The basal ganglia were noticeably smaller than the corresponding areas on a normal brain. A marked reduction in the nerve cells in this area was noted: in the lenticular nucleus, for example, a normal brain showed 69 glial cells, while in the patient's brain there were 127 glial cells. Whole fields were found consisting solely of glial cells, with no parenchymatous neurones. Focal scars were found in the caudate nucleus.

**POLIOMYELITIS.\*—*Diagnosis.***—In an analysis of 120 cases of poliomyelitis during the *preparalytic stage*, S. Baastrup (Ugesk. f. læger 96: 759 (July 19) 1934) found increased spinal fluid globulin in 91 and pleocytosis in 80. Every patient had some meningeal symptoms. Spinal stiffness with pain on bending forward appears to be a cardinal symptom of preparalytic poliomyelitis. Fever is also an essential, but nonspecific sign during this stage.

Julius Siegel (Wien klin Wchnschr 47.237 (Feb. 23) 1934) lists the symptoms of poliomyelitis during the preparalytic stage as slight rise in temperature, vomiting, headache, sore throat, and constipation forming a prodromal clinical entity. After a short symptomless period, a secondary stage is reached, during which a definite diagnosis should be made before the onset of the paralysis. During this phase of the illness rigidity of the neck, localized hyperesthesias, ataxic tremors, backache, weakness of legs, tenderness of nerve trunks, and profuse perspiration appear with varying degrees of consistency and constitute the symptomatic base on which the diagnosis should be made. Lumbar puncture should be performed in a child exhibiting many of these symptoms and a clear fluid with a lymphocytosis and a normal sugar content should arouse the strong suspicion of poliomyelitis.

**Second Attacks.**—As a rule, an attack of poliomyelitis confers an immunity against subsequent attacks; however, 14 cases of reinfection have been reported prior to 1934, and in addition thereto, 3 further instances of second attacks of poliomyelitis are presented. Reinfections must be distinguished from relapses. T. B. Quigley (J. A. M. A. 102: 732 (Mar. 10) 1934) suggests that second attacks occurring within 7 months be classified as relapses.

\* See also Section on PEDIATRICS

Thomas Moore (Brit. M. J. 2:166 (July 28) 1934) observed the case of a boy who had a residual weakness of the legs following an attack at the age of 4. Three years later he developed a mild, vague, febrile illness, and within a few days manifested a weakness of the recti muscles, and of the muscles of the abdomen and upper extremities. In the case reported by M. Tesdal (Norsk Mag. f. laegevidensk. 95:978 (Aug.) 1934), a quarter of a century elapsed between the two attacks. His patient had a paralysis of the legs as a result of a siege of poliomyelitis when 14 years of age. At 39, he suffered a bout of fever with weakness of the arms. Neurologic examination and spinal fluid study pointed to poliomyelitis as a diagnosis. This man was left with a residual paralysis of an arm. Quigley's case (*loc. cit.*) is the only one on record in which a reinfection was fatal. At the age of 7, his patient had been left with a paralysis of the deltoid from an attack of poliomyelitis. Two years later, she suffered from a bulbar paralysis from which she died. Autopsy showed axonal degeneration of the laryngeal nerves, and degeneration of the motor nerve cells of the pontine area.

**Prophylaxis.**—To protect against poliomyelitis, John Kolmer (Am. J. M. Sc. 188:510 (Oct.) 1934) is inoculating a group of children with a **vaccine** containing living virus. The preparation is devitalized with sodium ricinoleate. The complete procedure consists of a series of 3 subcutaneous injections; the first injection is a dose varying from 0.2 c.c. to 0.5 c.c., according to the age and weight of the child, varying amounts are given at each of the subsequent injections. One injection may be given weekly. The total amount of vaccine given in the 3 doses should not exceed 0.1 c.c. per kilogram ( $2\frac{1}{2}$  lbs.) of body weight. Kolmer believes that this procedure constitutes an effective vaccination against infantile paralysis.

**Treatment.**—Of 26 patients suffering from poliomyelitis, treated with **convalescent serum** during the preparalytic stage by H. Schlossberger and R. Krumeich (Klin. Wchnschr. 13:902 (June 23) 1934), 24 recovered completely and 2 were left with residual paralysis. None died. Of 201 patients who received the serum after paralysis had developed, 28 (14 per cent) showed improvement in the extent or intensity of paralysis, 25 (12 per cent) died, and the remaining 148 (74 per cent) showed no change in the neurologic status. These proportions of improvements and deaths are substantially the same in this group as in the reported series of untreated cases. For this reason, the authors, although strongly in favor of the use of the serum during the preparalytic phases of the illness, are skeptical of the value of this form of therapy in patients who have already shown paralytic symptoms.

Favorable results are reported by Gustav Torok (Med. Klin. 30.1093 (Aug. 17) 1934) in a series of 49 patients suffering from acute poliomyelitis treated by a combination of **auto-cerebrospinal fluid inoculation** and **convalescent serum immunization**. From 30 to 40 c.c. of spinal fluid were withdrawn every other day. Half of the amount withdrawn was injected intramuscularly on the day of the tap, and the remaining half was administered in the same way on the following day. This treatment was combined with the intramuscular injection of convalescent serum, or whole blood; the dose of the latter

was 30 to 50 c.c., depending on the age of the patient. These treatments were continued for from 8 to 12 combined injections, the longer period of therapy being used in patients who had already manifested paralytic symptoms

**BULBAR POLIOMYELITIS.**—Poliomyelitis is generally thought of as a disease of the spinal cord only. This, however, is not true; in a series of more than 1300 cases of infantile paralysis studied by E. Smith and H. Fineberg (*J. Pediat* 4: 590 (May) 1934), 29 per cent. were bulbar. Any part of the brain stem may be involved. Usually the infection centers about the medulla oblongata, but a case of the relatively rare pontine form is reported by P. Kiss and B. Hechst (*Monatschr. f. Kinderh.* 59: 418 (May 14) 1934). Their patient, a child, had hyperpyrexia, pain in the neck, diplopia, cerebellar ataxia, ptosis, and meningeal symptoms. Clinically, the case appeared to be one of meningitis, but the spinal fluid ruled out that disorder and suggested poliomyelitis. At autopsy this diagnosis was confirmed by the histopathology of the brain stem. The cells in the motor nuclei of the pons and neighboring tissues were destroyed in the manner characteristic of the pathology of poliomyelitis.

When a diagnosis of bulbar poliomyelitis is made, lumbar puncture is contraindicated. If for any reason a spinal tap is essential, it should be done very slowly and only a small amount of fluid withdrawn. Capillary hemorrhages, bulbar edema, and death have followed hasty spinal taps in cases of bulbar poliomyelitis. Nor is there any reason for employing a respirator, that instrument being of use only when the dyspnea is due to diaphragmatic, abdominal, or intercostal muscle paralysis and not when it is due to failure of the respiratory center in the brain stem.

The *treatment* of bulbar poliomyelitis recommended by Smith and Fineberg (*loc. cit.*) consists of application of **suction to the oral cavity** to free it from the accumulated mucus, **proctoclysis** of water at body temperature, **hypodermoclysis of dextrose** (5 per cent) in **physiologic salt solution**, and **nasal gavage**. The gavage should not begin until the fever has subsided. The solution used in this form of feeding is made by adding 1 egg and 2 ounces (60 c.c.) of sucrose to 8 ounces (240 c.c.) of milk. The amount of fluid introduced at each gavaging should be small—2 ounces (60 c.c.) at the first dose, gradually increasing to 8 ounces (240 c.c.) every 4 hours. **Postural treatment** is also important. At first the patient should lie with face downward on a hard mattress. When palatal function is restored, the patient may lie on his back, but no pillow should be permitted until the difficulty in taking semisolid nourishment abates. The head may be raised a little more every day.

*Difficulty in swallowing* is a common clinical complication of bulbar poliomyelitis. Two-thirds of the patients suffering from cranial nerve lesions in this disease have dysphagia, according to the analysis of case records made by M. B. Brahdly and M. Lenarsky (*J. A. M. A.* 103: 229 (July 28) 1934). This symptom usually clears up within a week, although in 5 of their 87 cases the dysphagia persisted for more than 3 weeks. The treatment of patients with difficulty in swallowing presents certain special therapeutic problems. The régime outlined by Brahdly and Lenarsky in such cases depends on the form of the dysphagia. Four clinical classes are recognized. (1) Paralysis of the soft

palate with regurgitation of food; (2) paralysis of mylohyoid with accumulation of food in the throat; (3) paralysis of the esophageal or pharyngeal musculature with vomiting; (4) paralysis of the vocal cords or external laryngeal muscles with coughing.

*Treatment* consisted of **suction** and **postural drainage**, **fluids intravenously**, **rectally**, and **subcutaneously**, and **nasal feeding**. To effect postural drainage the foot-end of the bed is elevated and the patient's head is turned to one side. **Gavage** may be administered by the ordinary nasal tube. If the inability of the patient to swallow persists, the feeding may be continued by means of the **Levin tube**. This is a catheter, about 4 feet long, with a velvet eye at the distal end. It is about as thick as a urethral catheter and is a useful method of nasal gavage in patients of this group. **Sedatives** should be administered as indicated, but **atropine**, being a respiratory depressant, *should be avoided*.

### **PROGRESSIVE SPINAL MUSCULAR ATROPHY.—Treatment.**

—The treatment of progressive muscular atrophy of spinal origin is unsatisfactory, according to E. Brand (Bull. New York Acad. Med. 10 289 (May) 1934). It should be directed at any causative factor which may be found. Tonic medication is advocated by M. Dubois (Schweiz. med. Wchnschr. 63:1093 (Oct. 28) 1933), and may be of some temporary value. **Strychnine** in doses of  $\frac{1}{30}$  grain (2.2 mg.) daily, the use of **elixir iron, quinine and strychnine**, 1 dram (4 Gm.) 3 times a day and also of **Fowler's solution** in doses of 5 or 6 drops 3 times a day may be of some value. Recently, P. Kiss and P. Meszoly (Monats f. Kinderh. 59 183 (Jan.) 1934) reported a case treated by **x-ray** therapy. He was given 875 r units over the spine, which was divided into 5 doses. Improvement began after the second treatment, and continued. During the sixth week and after the fourth treatment, muscle function returned and the atrophy disappeared. After 12 weeks the reflexes returned and some months after treatment the condition had not recurred. In view of this experience, it might be of value to try x-ray therapy in a large number of cases of this sort. **General hygiene, abundant rest and good food** are, of course, important.

**SUBDURAL HEMORRHAGES.**—These hemorrhages are much more common than is generally supposed. Were examination of the head made a routine part of every autopsy, many cases would be discovered which had never been diagnosed in life. Most of these cases are posttraumatic, but the trauma which precipitates the condition is often trivial. The present series reported by Timothy Leary (J. A. M. A. 103 897 (Sept. 22) 1934) represents an analysis of 50 cases of subdural hemorrhage. A disproportionately large number of the victims (54 per cent.) were alcoholics; this may be due to the fact that alcoholism often leads to falls and other traumata, or to the possibility that the cerebral edema associated with alcoholism favors rupture of the bridging arachnoid veins. None of the patients gave evidence of having a hemorrhagic diathesis.

In most of the cases (80 per cent.) a fall or blow on the head had preceded death. In 2 instances, bleeding had occurred into brain tumors, 1 patient had had

a fractured skull a year before death; in 3 of the alcoholics there was no history of trauma.

Subdural hemorrhage can arise from the rupture of vessels anywhere in the structures lining or abutting on the subdural space. The brain may be lacerated or contused after a head injury, thus producing subdural hemorrhage. The injured vessels are usually veins. Bleeding may be rapid, slow, or intermittent. **Operative intervention** is usually the only successful therapeutic method.

**TETANUS.—Treatment.**—Good results in the treatment of tetanus are reported by Karl Hempel (Klin. Wchnschr. 13. 482 (Mar) 1934), who combines **tribromethanol anesthesia** with large doses of **tetanus antitoxin**. Anesthesia is induced by the injection of tribromethanol; the dose begins at 0.08 Gm ( $1\frac{1}{4}$  grain) for each kilogram ( $2\frac{1}{5}$  lbs) of body weight, and is gradually elevated to 0.125 Gm (2 grains) per kilogram. Injections of the anesthetic are made daily. The wound is excised, and tetanus antitoxin is introduced around it. The antitoxin is also administered intravenously and intramuscularly, very large doses being employed. In a case cited, a boy weighing 20 kg (44 lbs) received a total of 500,000 antitoxin units intravenously and 240,000 units intramuscularly. The same patient also absorbed a total of 53 Gm ( $1\frac{3}{4}$  ounces) of tribromethanol during the course of treatment.

**Curare** appears to have a place in the treatment of tetanus. It is, of course, supplementary to **tetanus antitoxin** medication. In 2 cases reported by Louis Cole (Lancet 2 475 (Sept 1) 1934), curare appeared to have a beneficial effect in checking spasms and lessening rigidity. The preparation is given by injection, in severe cases it may prevent exhaustion and relax the mandibular spasm sufficiently to permit the administration of food, in such cases, curare permits the patient to be carried over a very critical period. Standardized preparations are not available, so that specific information regarding dosage cannot be given.

**TUBEROUS SCLEROSIS.**—J. S. Gottlieb and G. R. Lavine (J. Nerv. and Ment. Dis. 80 470 (Oct) 1934) reported a case of tuberous sclerosis in a 23-year-old female showing the usual epiloia syndrome, *e. g.*, mental deficiency, convulsive seizures and adenoma sebaceum, but, in addition, unusual changes in certain bones. X-rays revealed a peculiar mottling with indistinct islands of increased density, alternating with areas of rarefaction throughout the calvarium. The metatarsals and metacarpals, with their associated phalanges, showed periosteal thickening and generalized osteoporosis. The latter revealed a few small areas of marked rarefaction, suggesting small cysts. Curiously, the long bones, ribs and spine, other than in a spina bifida of the sacrum, were normal. Besides these bony changes, examination of the fundi revealed flat tumors or "phakomata." The retinal tumor of the right fundus had a fine capillary meshwork about its periphery which suggested that found in von Hippel-Lindau's disease. The puzzling bony lesions could not be adequately explained except possibly as due to either a neurotrophic or a chronic inflammatory process. The observation of Gottlieb and Lavine is valuable and suggests that x-ray examinations of the skeleton are indicated in the study of these cases.

**PSYCHIATRY.—DEMENTIA PRECOX.**—*Etiology.*—Discussion regarding the etiology of schizophrenia offers many divergent views. Toxic-infectious causes with protean manifestations, fundamental germ plasm defect, specially endowed nervous systems which break under environmental stress either infectious or the factors of early experience; all have their particular exponents. Those whose views are pessimistic point to the recent studies in heredity, especially where identical twins develop similar psychoses, to substantiate their belief. All study of mental cases is complicated by the two factors, *heredity* and *environment*. Certainly in monozygotic uniovular, similar twins, one factor may be disregarded. Several cases have been recorded but it is possible that not enough studies have been made to prove that perhaps only one of the twins may develop a schizophrenic breakdown. Where both develop the same psychosis, the occurrence is so dramatic as to attract attention. J. Kasanin (Am. J. Psychiat. 14:21 (July) 1934) reports a case in which one of identical twins developed dementia precox and the other remained well 8 years later. Rosanoff informed the author that of 38 pairs of monozygotic twins investigated for schizophrenia, there were 11 instances in which only one was affected. One of the cases reported showed similar environment and experiences up to the age of 16, when both twins developed impaired hearing. A. B., the patient, was more seclusive, interested in religion, wrote, and developed paranoid ideas, while C. D., the brother, was more alert and able to maintain better contacts with people. After graduation from high school the latter went to work with an uncle who was a successful mechanic. C. D. went to college and made good business adjustment. While not absolutely proven that these brothers were identical twins, it is most probably a fact. The report stresses the great importance of even slight change in environment on preservation of mental health.

A method of investigation to determine the relationship between blood grouping and schizophrenia as throwing some light on *heredity* is described by Morris Yorshis and Jacques Gottlieb (*Ibid* 13:1285 (May) 1934). The preliminary study indicates a problematical increase in group III for schizophrenics, also a trend for sons to follow the same group as fathers and daughters their mothers. This tendency is more marked than in normal cases.

In a series of 45 cases of schizophrenia studied by Jacob Kasanin, Elizabeth Knight and Priscilla Sage (J. Nerv. and Ment. Dis. 79:249 (Mar.) 1934), 60 per cent. of maternal *overprotection* was found, rejection in only 2 cases. Such overprotection is believed to extend into the adult life and hinder proper adjustments, sexual and otherwise. Biological inferiority serves as one important cause for the overprotection, as do such factors as unsatisfactory relationship of parents, thwarted ambitions, etc. A vicious circle is set up in the life of the schizophrenic child because, while he needs the extra care, the receiving of this care hinders development and emancipation from parents.

As a result of a study of schizophrenic patients and adolescent children to whom meaningless syllables associated with definite concepts were given as a basis for formation of new concepts, L. S. Vigotsky (Arch. Neurol. and Psychiat. 31:1063 (May) 1934) arrived at some interesting conclusions. His

method has been used a long time by Ach and others. Four types of thinking were evident:

1. Collective, in which various objects are grouped together as if they formed a collection composed of different objects united to each other by certain relationships—such as a collection of things or objects of various colors, or various forms.

2. Chain complex thinking.

3. Associative complex thinking.

4. Pseudocomplex chain thinking.

Comparison of the schizophrenic's thinking with the various types indicated the degree of regression. There is similarity but by no means identity between the type of thought of a schizophrenic and the child. In the patient there is a breaking of the psychologic systems which lie at the basis of concepts; the meanings of words have become changed.

As a working hypothesis, it is stated that the ability to form concepts is fundamental for an integrated personality. The first stage involves ideas of physical causality, the second consists in secondary changes in other psychologic functions, while in the third stage there develops a world outlook, cognition of one's self and one's environment. The schizophrenic fails at the third stage. Regardless of etiology, disintegration of personality follows definite psychological laws. Schizophrenia is characterized by loss of psychic energy and asthenic habitus. Jung was the first to draw comparison between schizophrenia and dreams, saying, "if a man could walk and talk in his dreams his total behavior would be in no way different from that of a patient with schizophrenia." Pavlov has recently stated that the most probable physiologic cause of schizophrenia is the overdevelopment of the process of the inner inhibitions, which are also overdeveloped in hypnosis and sleep. The biologic purpose of sleep and inner inhibitions consists in cessation of contacts with the outside world; the comparison of a patient's loss of contact with the outside world is evident. Thus, schizophrenia is but an expression of the protective forces of the organism reacting with inner inhibitions to the weakness of the central nervous system.

**Pathology.**—The case report by Milton H. Erickson (*Am. J. Psychiat.* 13:1349 (May) 1934) is that of a schizophrenic from profound stupor to apparent social recovery, with detailed study as suggested by R. G. Hoskins (*Arch. Neurol. and Psychiat.* 30:388 (Aug.) 1933) as part of a cooperative research in schizophrenia. The period involved 7 months' study of psychiatric, psychologic and physiologic findings. Three distinct psychiatric states—stupor, recovery from stupor, and apparent recovery from psychosis. During each some definite concomitant physiological changes were found, the variations from the normal corresponding in both spheres. There was also a possible etiological factor in environment before onset, but this is not discussed as a part of this report. Likewise, an endocrine factor may have had some bearing. Whatever the real basis, the study is valuable evidence of organic dysfunction.

**Symptoms and Diagnosis.**—In a study of schizophrenic traits in the functional psychoses and in normal individuals, 100 traits commonly considered as schizophrenic symptoms were chosen by James Page, Carney Landis and S. E.



Katz (*Ibid.* 13: 1213 (May) 1934) and these were submitted to various psychiatrists until 50 were agreed upon as most typical.

Prefer group sports to taking walks alone.  
 Have a limited range of interests.  
 Find it difficult to concentrate.  
 Feel different from other people.  
 Worry excessively over unimportant details.  
 Blame yourself for your misfortunes.  
 Mind is generally clear.  
 Are emotionally disturbed for long periods.  
 Are easily confused and embarrassed.  
 See things that other people cannot see.  
 Have thoughts of doing violence to members of your family.  
 Are indifferent towards the world in general.  
 Are often in conflict with your environment.  
 Take pride in your physical appearance.  
 Tend to be carefree rather than serious-minded.  
 Are shy and timid.  
 Have feelings of guilt or sinfulness.  
 Find it easy to make decisions.  
 Are a good loser.  
 Worry excessively over humiliating experiences.  
 Are sensitive to criticism.  
 Desire to change the order of the world.  
 Often occupied with your own thoughts.  
 Enjoy being alone.  
 Believe people are after you.  
 Think it possible for other people to influence your actions  
 Are very tactful  
 Prefer an adventurous life to a quiet home life  
 Feel physically inferior to friends.  
 Desire to have lots of friends.  
 Have lots of faith in human nature  
 Feel that life is a dream  
 Have feelings of inferiority  
 Feel nervous in the presence of the opposite sex.  
 Are critical of others  
 Day-dreams a lot.  
 Are fussy about food  
 Dislike to have your faults revealed  
 Feel compelled to do certain things  
 Can read other people's thoughts  
 Emotions change frequently without cause  
 Feel mentally inferior to friends  
 Are talkative and unreserved  
 Are often absentminded  
 Troubled with religious matters  
 Feel misunderstood.  
 Hear voices that other people cannot hear.  
 Feel lonely even when with people  
 Do things without knowing why you do them.  
 Are touchy on various subjects

A questionnaire was then submitted to 100 manic-depressive patients, 125 schizophrenic, and 240 normal persons. The manic-depressive were interested, responded promptly and decisively. The schizophrenics were only mildly interested, inclined to be apprehensive and hesitant. Their attitude was guarded and suspicious. The normal and the schizophrenic possessed on the average the same number of schizophrenic traits, 18 and 17.6, respectively. The manic-depressive groups showed only 14 of these traits. It appears that normal individuals possess somewhat different traits than psychotic persons, but in general all groups tend to have the same personality traits. Only 8 traits were found to be of differential value between schizophrenics and manic-depressives

1. Believe people are after them
2. Feel that life is a dream
3. Hear voices that other people cannot hear.
4. Are fussy about food
5. Enjoy being alone.
6. Are poor losers
7. Desire to change the order of the world
8. Desire to have but few friends

This analysis fails to reveal a dichotomy of personality types between schizophrenic and manic-depressive patients. Either the hypothesis is incorrect or the questionnaire method is not a valid way to apply it. The lack of agreement regarding personality types is perhaps due to one group interpreting personality as an organized whole or a gestalt, while another group interprets personality as a sum of traits.

Personality is an organized whole rather than the sum of its parts, the whole is independent of its parts, but its parts are not dependent upon its parts.

In a discussion of crimes of unintelligible motivation as representing an initial symptom of an insidiously developing schizophrenia, with a study of the comparative effects of penitentiary *vs* hospital régime in such cases, A. W. Hackfield (*Ibid.* 14: 639 (Nov.) 1934) states that whenever a crime is committed for which there is no evident motive, the question of incipient schizophrenia in the perpetrator is of the utmost importance. If such a diagnosis can be established, the disposition of the case and the complexion of the crime are altered.

Such criminals treated medically may show good remissions and be prevented from deterioration. When given major sentences, such incipient cases rapidly deteriorate and cause prolonged financial burden; if untreated, they are a menace to the community and often commit major crimes later.

If nonpsychotic, the stress and strain of penal life will never precipitate a major psychosis. It is often a very difficult problem to determine an incipient schizophrenia, whereas a full developed psychosis presents no special difficulty.

To disregard the relationship of psychoses and crime is to acknowledge backwardness of a community. The borderline cases are the most difficult and the most frequently encountered.

The incipient schizophrenic and the unemotional psychopathic personality of the moral insanity type (the criminal in the true sense of the word) are the two classes most often met. The emotionally unstable psychopathic individual is not

of the group lacking motive. The legal and medical questions here become technical and the differential diagnosis between major psychoses in which there is intellectual impairment and the psychopath in which there are subconscious motives have led to much fruitless discussion.

Fleck is quoted as showing that in cases where crimes were committed by schizophrenics, the disease had been present for a long time and was directly the expression of the psychotic process. Brun in a study of 716 schizophrenic cases found that 14.5 per cent. are criminal at some time. Pighini found 50 per cent. of the inmates of an institution for the criminal insane to be unmistakably "dementia precox." The offenses may be of the basest sort. During the prodromal stage the incipient case's emotional life may be dominated by a shrewd and calculating coldness. Inhibitions are lost if once he has the desire to dispose of a fellow human. In the incubation period, the patient may commit a crime on the slightest provocation; a brother murdered a sister because of her immoral conduct; a girl strangled her fiance because her employer discharged her.

Only by prolonged observation of months in a psychopathic hospital can a satisfactory study of these early cases be made. Here his reaction to fellow patients, to work, to commitment and study must all be taken into consideration.

Grabfield, in 1914, reported that high thresholds were found constantly in patients with dementia precox as a result of faradic current stimulation. This he attributed to "general nervous irritability." The work of P. E. Huston (Arch. Neurol. and Psychiat. 31:590 (Mar. 1934)) has failed to confirm the former investigator's findings, *i. e.*, he noted no important differences between normals and schizophrenics. A very slight difference in his first test disappeared at the second and this he interpreted as indicating a slower rate of adjustment to new situations by patients suffering from dementia precox.

H. Freeman (*Ibid.* 30:1298 (Dec.) 1933) made a study of the sedimentation rate of the blood in schizophrenia in the hope that by utilization of the sedimentation rate, a means of detecting an organic background for schizophrenia might be found. Other investigators had reported various results, *e. g.*, that the rate in this condition was "retarded, normal, or increased." To make the study as conclusive as possible, 47 male patients with a diagnosis of dementia precox were chosen and 50 normals taken as controls. The patients were classified as to type and freedom from infection. Three tests were made at intervals of 3 months. There was no diurnal variation in rate and temporary venous stasis had no effect. Age or period of hospitalization appeared to be of no significance.

**Treatment.**—Wallbum's work showing an increase in antibody formation after administration of manganese stimulated several investigators to research regarding the effect of manganese on dementia precox patients. R. G. Hoskins (J. Nerv. and Ment. Dis. 79:59 (Jan.) 1934) reviews the results of 6 studies as well as his own. The manganese was given orally and intramuscularly. A group of 30 male patients varying in age from 17 to 52 years, who had been hospitalized from 1 to 24 years, were studied over periods from 19 to 107 days. Careful records of weight, basal metabolism, blood-pressure, blood findings, etc., were compared before and after treatment. The results showed no change in

physical or mental symptoms. Probably the occasional mental improvement of other investigators was due to unintentional psychotherapy.

**MENTAL DEFICIENCY.—*Social Significance.***—E. O. Lewis (J. Ment. Sc. 79:298 (Apr) 1933) states that mental deficiency is nothing but a variation from the normal in the range of mental equipment, and since the range of normal variation is not known, it should not be assumed that a mental defect is necessarily an evidence of abnormality. Mental deficiency that is abnormal belongs to a definitely organic pathologic group, which presents structural disease and abnormalities of the central nervous system. These cases should be called *pathologic types*. The person with mental deficiency who simply varies in his intellectual equipment from his fellow man should be called a *subcultural type*. Lewis points out that the deficiency is only an extreme example of normal variation of mental endowment. There is no definite cleavage, but a close biologic kinship, between this group and the mass of normal persons. This is altogether different from the case of the so-called pathologic defective. A classification such as suggested by Lewis offers an opportunity to understand the social problems involved, since a great majority of defectives in the community belong in the subcultural group, while most cases in the abnormal class belong in the lower grades of deficiency, idiots or imbeciles. Heredity is a more important factor in the production of the subcultural types than in the production of the pathologic types. When several defective persons are found in one family, they are usually of the subcultural types.

***Sterilization of Mental Defectives.***—The Report of the Departmental Committee on Sterilization (H. M. Stationery Office, London, 1934; Am. J. Psychiat. 14:464 (Sept) 1934) states that the number of persons for whom on account of mental defect or hereditary physical defect or mental disease, sterilization should be considered, is not large. Sterilization is one of the means of race improvement, but it is not a panacea, nor is it a penalty. It is "in effect a therapeutic measure."

The Committee made a number of Principal Recommendations among which are the following:

I Subject to the safeguards proposed, voluntary sterilization should be legalized in the case of

(a) A person who is mentally defective or who has suffered from mental disorder

(b) A person who suffers from, or is believed to be a carrier of, a grave physical disability which has been shown to be transmissible, and,

(c) A person who is believed to be likely to transmit mental disorder or defect

II Before sterilization is sanctioned in the case of a mental defective, care should be taken to test his or her fitness for community care

III Mental defectives who have been sterilized should receive the supervision which their mental condition requires

IV The operation of sterilization should only be performed under the written authorization of the Minister of Health (England), in regard to which the following procedure should apply:

(a) Application for the authorization should be supported by recommendations in a prescribed form signed by two medical practitioners, one of whom should, if possible, be the patient's family doctor and the other a practitioner on a list approved by the Minister. No medical practitioner should sign a recommendation unless he has examined the patient

(b) The Minister, on receipt of the recommendations, should be empowered to require any necessary amendment of the forms and to cause the patient to be specially examined if it is considered advisable.

(c) In order to deal with difficulties that may arise in connection with applications on behalf of persons suffering from, or believed to be carriers of, inherited disease or disability, the Minister should be empowered to appoint a small advisory committee consisting partly of medical practitioners and partly of geneticists to whom doubtful cases could be referred.

(d) The hospital authorities or (in case of operations performed elsewhere) the operating surgeon should be required to notify the Minister when the operation has been performed.

(e) In all cases in which the patient is capable of giving consent, he should sign a declaration of willingness to be sterilized, and one of the two medical recommendations should include a statement that the effect of the operation has been explained to the patient and that in the medical practitioner's opinion he is capable of understanding it. If the practitioner is not satisfied that the patient is competent to give a reasonable consent, the full consent and understanding of the parent or guardian should be obtained. If the applicant is married, he or she should be required to notify the spouse of the application.

(f) In the case of persons who have suffered from mental disorder, sterilization should not be permitted without a recommendation from a competent psychiatrist, who should be required to certify, after examining the patient, that, in his opinion, no injurious results are likely to follow.

(g) The procedure should at all stages be treated as strictly confidential.

V Medical practitioners, in making recommendations for sterilization, should have protection similar to that accorded to them in respect of certificates given under the Lunacy and Mental Treatment Acts.

These recommendations are apparently the result of careful study of the problems involved, and although adapted primarily to meet the requirements of England, can be used as a model for sterilization legislature in this country.

**MONGOLISM.—Etiology.**—A J Rosanoff and C V Inman-Kane (Am J Psychiat 13 831 (Jan ) 1934) in an article dealing with the relation of premature birth and under-weight condition at birth as related to mental deficiency, state that there are some abnormal conditions which do not seem to run in families and are, therefore, not strictly hereditary, but which can, nevertheless, be shown to be caused by germinal factors. A striking instance in point is that of mongolism. Among monozygotic twins, if one is a mongol, the other is quite invariably also a mongol. Among dizygotic twins, it is quite regularly observed that if one is a mongol, the other is normal. Mongolism is scarcely ever found in more than one member of a familial strain. Moreover, mongols are sterile and short-lived, so that direct inheritance is practically out of the question. There is reason for thinking that sclerotic and atrophic changes in the ovary can so injure an ovum during the germinal period as to produce mongolism.

A J Rosanoff and L M Handy (J A M A, 103 1805 (Dec 8) 1934) state there is definite correlation between the incidence of mongolism and the age of the parents. An attempt is made to show, however, that the real etiologic factor is the *age of the mother*, that of the father having only an indirect bearing by reason of being in statistical correlation with the age of the mother. Similarly, the size of the family, the order of birth, "uterine exhaustion," and so on, play no part in the etiology of mongolism, they stand out in the statistics only by reason of their correlation with the one real factor; the age of the mother. Mongolism is more common among boys than among girls. This finding is so constant

as to force one to assume that, although injury to the ovum is the essential cause of mongolism, the spermatozoon is not without its influence. The X-chromosome in the female-producing spermatozoon seems in some cases to have the power of protecting an injured ovum against its tendency to develop into a mongolian child. It is pointed out in this connection that mongolism varies greatly in the severity of its manifestations and, on the whole, is milder in girls than in boys, possibly owing to partial protection by the additional X-chromosome. All the known facts concerning mongolism seem to point to some condition of the *ovary* as underlying its pathogenesis. No systematic pathologic investigation of the ovaries of women who have given birth to mongolian idiots has been made, to the authors' knowledge. Coarse or diffuse lesions seem to be excluded as a possible cause. All available evidence seems to justify the speculation that foci of tissue change—perhaps scars—marking the sites of old ovulation are the cause of the trouble.

**NEUROSES.**—The *diagnosis* and *treatment* approach to the neuroses is presented by R. H. Young (Nebraska M. J. 19. 179 (May) 1934) in an article entitled, "Practical Considerations of Body Complaints in Absence of Organ Pathology." In recognition of the neurosis he enumerates certain considerations upon which attention should be focused: (1) The facts as stated by the patient and how such facts are presented, whether with much or little exaggeration, etc.; (2) conditions under which symptoms developed, *i. e.*, environmental situation at the time, (3) cause of development, noting the situational facts during development of symptoms, (4) the end-result in terms of the setting, emotional, ideational and environmental, in which the present complaints exist, (5) mental status, especially with regard to the presence of (*a*) anxiety, (*b*) invalid state of mind (resignation), (*c*) depressive state, (*d*) twisted or bizarre type of complaint, accompanied by odd personality make-up, such as sensitivity, suspiciousness, etc.

Attention to these considerations, in addition to a careful physical examination, should place the physician in a better position to evaluate symptoms that are psychogenic in origin. In *treatment* he stresses a clear and simple presentation of the relation of the emotional factors to the symptoms when such is evident, and urges the avoidance of attempts to reduce the complaints to an organic basis, *forgetting the individual*. The physician should educate the patient so that in situations of emotional strain there is a corresponding action upon the body organs giving symptoms, but not necessarily irreparable pathology. The immediate environmental strain should be pointed out so that the patient may cope with it. An opportunity should also be given the patient to express feelings of guilt and incompetence. The physician should attempt "to break up the adhesions which the habits of invalidism have formed."

Medicine should be given sparingly, but if given, the reason therefor should be clearly stated. The twisted bizarre personality should be placed in a hospital with psychiatric facilities, because there may be a more serious mental disorder in the process of formation, such as schizophrenia.

The value of **psychoanalysis** as an intensive type of treatment for body symptoms of neurotic origin is shown by A. D. Finlayson (Ohio State M. J. 3:94 (Feb.) 1934). In the case described, a multitude of physical manifestations responded excellently to psychoanalytic treatment after many other approaches over a period of 8 years had been unsuccessful. The patient was made aware of many unconscious anxieties, fears, inhibitions and feelings of incompetence by the method of free association and his childish anxieties were transformed into a more acceptable adult expression. This released the emotional energy exerting itself through the autonomic system upon the body organs, and a return of health resulted.

Approach to the problem of the neuroses from an angle other than psychogenesis is considered by A. W. Rowe and H. M. Pollock (Endocrinology 17:658 (Nov-Dec.) 1933). An analysis of 140 cases of psychoneuroses and 110 cases of psychoses indicated that three-fourths of this group presented some form of *endocrine disorder*. The authors, however, disclaim any effort to establish any causal relationship between mental disease and endocrine disorder. They do regard the selective character of the associates as suggestive and warranting further and more extended study.

**PSYCHOLOGY, ABNORMAL.**—In an article bearing upon clinical problems, entitled, "Meaning of the Term Abnormality in Psychology," E. B. Skaggs (J. Abnorm. and Social Psychol. 28:113 (July-Sept.) 1933) admits the difficulty of clear cut definitions in the biological sciences, and stresses the need for it. He describes the present confusion of the concepts of abnormality, some are in terms of the inner man or mind, others in terms of the outer man or behavior; some accept a social criterion of abnormality, others a biological; some define abnormality as a structural disorder, while others define it as functional; some define it in terms of some ideal or arbitrary standard of perfection, whereas others define it relative to a statistical norm; some define it in quantitative terms, whereas others insist on a qualitative definition.

With this in mind, the author does not pretend to attempt an adequate psychological definition of abnormality, but offers a few constructive suggestions toward that end.

Man is both a biological creature and a social creature, hence, any adequate psychological definition must allow for both these concepts of man and his behavior. He points out that a person might be biologically normal and socially abnormal, and *vice versa*. Abnormality, he believes, must of necessity be a qualitative and not a quantitative concept at the present time. In other words, the term abnormal means more than that which is suggested by the terms sub- and super-normal. An abnormal person is not one who has simply more or less of a given capacity or trait. *He is, rather, one in whom a balance between many delicate parts has been upset; one in whom an elaborate integration between mental concepts and drives has, to some extent, at least, broken down.* He is a personality in whom the constituent parts are not well integrated. Skaggs would, therefore, reserve the terms sub- and super-normal for expression of quantitative variations. He would call a feeble-minded boy subnormal, and one with a

very high intelligence quotient supernormal. Either might be abnormal, though not necessarily so.

Since cases of abnormality seem to differ from each other in degree, and since we have no way of expressing quantitatively the multitude of interrelationships between the factors which constitute personality, the author concludes that abnormality is and must be a qualitative concept.

**PSYCHOANALYSIS.**—In a discussion of the question of *addiction to surgery*, K. A. Menninger (Psychoanalyt. Quart 3 173 (Apr.) 1934) shows how the motive which brings the patient to operation may lie very deep in the unconscious mind. Especially in the field of plastic surgery does one see a morbid neurotic craving on the part of the patient to have something done even though no physical discomfort exists. In other surgical fields, also, the symptoms complained of may represent the focus of a deep underlying conflict, where surgery only begins to reach the seat of the trouble.

It is not denied by the author that surgery sometimes may give relief in a neurosis or psychosis, but such relief is both inconstant and transitory in its effects.

Of these unconscious motives for surgery one of the most common and obvious is the avoidance by the patient of something feared more than surgery. A case cited is that of a woman who repeatedly postponed her marriage by an operation. A second motive is that of the patient wishing to submit himself to the hands of an incisive, firm, dynamic individual, who represents the father and upon whom he can be dependent. The pain and discomfort of operation is a small though necessary sacrifice for such a patient to bring about this highly desired situation. Again, an operation may fulfill a deep unconscious wish for a child, especially on the part of women, who still carry a childish belief that children are born as a result of operation. Finally, a fourth motive is that derived from the unconscious wish to be castrated. In such a wish there are two elements (1) the need for punishment, and (2) the erotic capitalization of it.

In its most obvious form are seen many patients demanding removal of one or both testicles in order to reduce their erotic desire. From this as the nucleus, a diffusion of this motive will be seen extending to operation in all parts of the body to achieve the same results.

The author also points out that these are often not only neurotic compromises in themselves, but an attempt of a disintegrating personality to ward off a psychosis. He regards the compulsion to submit to surgical operations as a form of localized self-destruction or partial suicide. It would differ from partial suicide in that the whole organism was being saved by sacrificing a part; that the responsibility of the act was shifted to a second party; and that opportunities for secondary capitalizations (*i. e.*, obtaining love and pity) were greater.

The author would have the surgeon cognizant of some of these mechanisms and utilize a psychiatric consultant more freely.

M. W. Peck (New England J. Med. 210 207 (Jan 25) 1934) discusses the application of certain psychoanalytic concepts to general psychotherapy. He stresses the value to any physician of understanding the phenomenon of trans-



ference, or what has long been known as rapport between physician and patient. Its proper appreciation and use may have a far reaching constructive effect. In the past it has been looked upon with disdain as being too unspecific and too unscientific for use by a reputable physician. But this viewpoint has been changed. Rapport well understood and well utilized is a valuable weapon in the management of ill people, especially the neurotically ill. It may be used to foster independence and return to health, and only when not well and honestly utilized, does it foster dependence and helplessness on the part of the patient that lead to poor results.

The author points out that psychoanalysts are the first physicians who have had the courage to deal with the negative transference of patients expressed in childish doubts of the value of the treatment, open hatred and criticism of the physician. This hostile rapport also may be turned to good account if properly dealt with, because it offers a situation in which the patient can be shown clearly his emotional problems at close range.

Peck also stresses the use of passivity as a therapeutic agent, *i. e.*, a willingness to listen to the patient rather than always giving advice or telling him what he should do. This permits the patient to have the courage to express himself and allows the physician to see hitherto hidden sources of conflict and friction, and their relation to the disease under treatment. This, of course, may require a minimum of skillful guidance in order to bring out especially things which the patient wishes to talk about but is unable to put into words, and also what he does not wish to face squarely and tries to evade. The result can be very beneficial in that hitherto diffuse and confused thoughts and feelings on being expressed are clarified to the speaker and are taken back into himself with more insight and order than before. In this way a more constructive help is given without too much emotional cost to the physician, and the results are better and more lasting because the patient has seen something of himself rather than having only been told about himself. The results of insight obtained in this way are much more effective. The author stresses that skilled psychotherapists are needed for the more difficult problems, but that just as some minor surgery must be done by the practitioners, so must some of the minor psychiatry be done by them, and offers in his article suggestions for its performance.

**PSYCHOPATHIC PERSONALITY.**—In an article by B. Karpman (*Arch. Neurol. and Psychiat.* 32: 577 (Sept.) 1934), discussing certain psychopathies, especially sadism, masochism and fetishism, the author shows their relation to neurosis and criminality, and states that he has long suspected that what is now regarded as constitutional psychopathy may, on more careful observation and study, eventually turn out to be but a particular form of sadomasochistic neurosis, with greater emphasis on sadism than masochism and with but little, if any, sense of guilt developed. As in other neuroses, the sufferer seldom wishes to get rid of his neurosis, but only of the distressing symptoms. Like other neuroses, these too have their beginning in early childhood when circumstances induce quantitative distortion of the love and hate reaction. The author calls them

a form of psychosexual infantilism, and stresses the environmental influences as the etiological factor.

In many ways sadism, masochism and fetishism resemble obsessional neuroses. The phantasy life is exuberant, in which intense hatred is expressed, the latter usually linked with sexual activity. Nevertheless, the end-result is flight from normal sexuality.

The author suggests that some of these cases are curable by **psychoanalysis**, as are the neuroses, and even though some have not been cured, this may not mean that they are not curable, but only that the proper approach has not been found. He believes that **psychotherapy** offers an approach to treatment.

While treatment at present has its limitations, the author offers suggestions for *prophylaxis*. "These must be directed to two sources, the family and the school. Punishment only tends to heighten the child's sadistic reaction. Servants and educators frequently take vengeance on the children for the oppression to which they have to submit from the children's parents. Especially reprehensible are those forms of abuse which are draped under the ethical mantle of pedagogy. It is certain that only love can educate. Parents and educators who beat the children entrusted to them, commit a crime toward the children and toward the state because such treatment unfits the children for life.

"Unfortunately, parents have no idea how early a child receives sexual impressions. It is the parents' duty to guard the children from all impressions which may poison their phantasies. Physicians should work toward enlightenment in this respect and concern themselves with the mental hygiene of the nursery. Intercourse of the parents which is overheard, scenes of strife and reproaches for unfaithfulness made through jealousy may lay the foundation of a sadomasochistic or fetishistic neurosis.

"The overwhelming role that jealousy plays in the psychogenesis of sadomasochism and fetishism cannot be overestimated. Hence, the best prophylaxis for these paraphilias lies in education. What society needs is a campaign against envy and jealousy. Everything should be excluded from the family circle which could justifiably excite jealousy. Weak and sickly children are often coddled. This leads to jealousy of the healthy child toward the sick one, and also sets an example of the advantage to be obtained from illness. The love of parents and educators must be impartially distributed.

"The forbidding of onanism and the punishment of infantile sexual play readily produce an attitude of hatred in the child toward the parents and toward all society. The child's right to his sexuality, which is now recognized as always present and necessary to his development, is not yet well established. Parents and educators would do well not to trouble themselves over the sexual life of the child if it does not transgress the canon of the normal."

As yet, little is known of the inner psychic life of even normal children. However, from studies of cases, these suggestions are indicated as prophylactic measures against relieving the suffering occasioned by the maladjustment in the biologic and psychic evolution of man, of which psychopathies are examples.

**PSYCHOSES.—Pathology.—Lipoid Metabolism.**—The cholesterol content of the blood in early *dementia precox* is decreased by about 25 per cent., according to J. S. Sharpe (J. Ment. Sc. 80:75 (Jan ) 1934). Later there is an increase by about 30 per cent., as chronicity advances, and it remains at that figure. This may be due to a hyperactivity of the suprarenal glands.

In *melancholia* the blood cholesterol is slightly on the high side, but the variations are small, the coefficient of utilization is low, together with deficient oxidation and low metabolic activity. *Recurrent mania* cases show very high blood cholesterol, particularly during an acute attack. The cyclic nature of the condition seems to suggest some derangement in metabolic activity, probably centered around the suprarenal glands, as evidenced by the blood cholesterol increase. There exists in the blood in certain melancholic and confusional states, a powerful depressor substance having a choline-like action on the isolated frog heart. This substance is antagonized by adrenalin.

Normally, the depressor substance is in such small concentration as to be almost undetectable; called "cholinase." It is deficient or completely absent in *melancholia*. The clinical picture of these cases is that of hypotonia.

**Treatment.**—Following favorable reports of other investigators regarding the effects of **hematoporphyrin** on the psychoses, E. A. Strecker, H. A. Palmer and F. J. Braceland (Am. J. Psychiat. 13:1157 (May) 1934) undertook a research problem in which 37 patients were studied; 23 of this group were diagnosed manic-depressive psychosis, 8 as involutional melancholia, and 6 schizophrenia. The method of administration was oral and intramuscular. Of this group, 25 showed definite improvement, mentally and physically. Details regarding pharmacology are still lacking. It is known that hematoporphyrin has a marked photosensitizing effect when injected into the human body. It has also been shown to produce alteration in the blood electrolyte values, chiefly calcium.

**DEPRESSIONS WITH TENSION.**—A group of depressed cases in first attack in which tension was an outstanding symptom are presented by Wendell Muncie (Arch. Neurol. and Psychiat. 32:328 (Aug ) 1934). These were well-adjusted personalities before onset, who were able to get their own way, and appeared aggressive, self-reliant, stubborn, rigid and inflexible. All showed undue attachment to parents or parent substitutes. They took responsibility seriously and their activity was the release for tension. They were dependent upon environment and inclined to place blame for failures outside themselves. Possibly the sexual element was an etiological factor in some of the cases but, as a rule, it was symptomatic of pre-existent general tension without special sex content.

The *prognosis* was doubtful and the *treatment* difficult because these personalities were not willing to admit cause, to adjust habits to environment or to face their problems with decision. This type of patient is not content to remain in the hospital or to accept supervised treatment. Small doses of **barbital** are advised, **continuous baths**, **belladonna** and **alkalis**, **hydrochloric acid** as indicated. The Jung association tests, psychogalvanic and Rorschach tests and analysis of dreams are helpful in determining the causes of the tension. The termination is by lysis.

**MANIC-DEPRESSIVE PSYCHOSIS.**—*Treatment by Psychoanalysis.*—Freud first outlined the problem of manic-depressive psychoses in a comparison of mourning and melancholia. Other authors have added varying theories, but all have traced the origin to “conflicts arising in, or at least impelled by, the pre-œdipus stage of sexual emotional development, though not all are convinced that this is the only factor, and some, at least, believe that inheritance plays a rôle.” Only about 17 case reports of *treatment* have been published. The case reported by C. A. Neymann (J. Nerv. and Ment. Dis. 80 24 (July) 1934) was that of a brilliant young chemist, 37 years of age, without any decided psychopathological strain, except for a cousin who was a schizophrenic. The patient had had 11 depressed periods, the first at the age of 20. They were associated with overwork, responsibility approaching marriage at 25, and at several of these episodes, serious suicidal attempts were made. Analysis with dream study follows in some detail. The yearly sequence of a depression was averted and the family consider his psychic make-up has undergone a miraculous change.

**SENILE PSYCHOSES.**—In a paper “Concerning Pick’s Disease,” E. Kahn and L. J. Thompson (Am. J. Psychiat. 13.937 (Mar.) 1934) discuss the pathology, clinical symptomatology and differential diagnosis of a form of presenile dementia first recognized and described by Arnold Pick, of Prague.

Grossly, the brain has the appearance of diffuse cortical atrophy, with circumscribed areas of intense atrophy in some of the convolutions being so distinct as to be seen readily by the naked eye. These intensely atrophic areas are not symmetrical and are usually more marked on the left hemisphere. The prefrontal and the temporal lobes are most frequently affected. Microscopically, there is seen a destruction and degeneration of ganglion cells in the first three layers. There are some compensatory hypertrophy and regressive changes of the neuroglia. Senile plaques and fibril changes as well as arteriosclerosis are absent. Clinically, 2 types of Pick’s disease have been described. In the one a characteristic dementia is noted and in the other the dementia is accompanied by aphasia. Early in the course of the disease there occurs a loss of ethical standards and perceptions, together with neglect of the formalities and niceties of social intercourse. Inattention, carelessness in habits, and a loss of the ability to use memory come next. As the disease goes on, patients become child-like, get lost easily, and give themselves to purposeless, repetitious movements and acts. They are emotionally unstable and hyperactive for a time. Finally come the end-stages of complete disorientation, loss of memory and inertia, leading to confinement in bed and death following incontinence and loss of strength.

This disease occurs more frequently in women than men. The average age of onset is in the fifth decade. The duration of the illness is from 2 to 4 years.

*Diagnosis* is based on an interpretation of the clinical symptoms aided by encephalographic findings of brain atrophy in the frontal and less often the temporal areas. Neurologic studies are usually negative, with the exception of aphasia in that particular type.

Pick’s disease must be *differentiated* from dementia paralytica, arteriosclerotic brain disease, brain tumor and Alzheimer’s disease. In *dementia paralytica* a neurologic examination and serologic studies should make the differentiation.

*Arteriosclerosis* can be determined clinically and by ophthalmologic findings. The history will show the arteriosclerotic to have attacks of vertigo and periods of confusion which are not featured in Pick's disease. *Brain tumor* can be ruled out by careful neurologic study enforced by encephalography. *Alzheimer's disease* is the most difficult disease to rule out. In this disease there is a more noticeable and complete early memory loss. There may be focal signs and convulsions. Encephalography offers differentiation, for in Alzheimer's disease broad strips of air are seen over the whole convexity, while in Pick's disease the air is confined to the frontal and temporal regions.

The authors do not mention therapy, because nothing of a specific nature has been found effective. The medical problem is one of general nursing care and symptomatic treatment.

**TOXIC PSYCHOSES.**—Marihuana is the name applied to a cigarette preparation of the hemp plant, which has an active principle, *cannabis sativa*. These cigarettes are popularly known in the United States as reefers. Walter Bromber (Am J. Psychiat 91:303 (Sept) 1934) has studied the effects of smoking these cigarettes in patients admitted to the psychopathic ward of the Bellevue Hospital in a state of *Marihuana intoxication*. Three clinical groups of cases were observed: (1) Acute intoxication; (2) emotional reactions to intoxicating features; (3) toxic psychosis due to admixture of drug effects and basic psychosis.

In acute intoxication, time appears to be lengthened. Subjective reality is heightened while objects in the environment appear less real. Consciousness is disturbed and there is difficulty in remembering things. Feelings of unreality may even lead to panic states in hysterical and schizoid individuals. An elated mood with periods of sudden boisterous laughter may occur. While intoxicated, persons may do things impulsively and have "an irresistible impulse toward wilful damage." They may have acute hallucinatory and delusional experiences. They may be in a state of acute mania. The drug is considered a "breeder of crime" only when used by psychopathic types in whom the drug releases the inhibitions on anti-social tendencies. The end-stages of prolonged use of this drug are not seen in this country. These are in the form of emotional and intellectual deterioration.

A tolerance to marihuana is not developed and a withdrawal of the drug causes no symptoms. Mental symptoms clear up readily when the toxin is eliminated, except in those cases in which an underlying schizophrenia or other psychosis is present. The treatment is directed toward protection of the patient during his mania or confused state. **Immediate withdrawal** of the drug, **bed rest**, and proper **elimination** are indicated.

**PSYCHOSES WITH ORGANIC DISEASES.**—*Diseases of the bony framework*, such as osteitis deformans and osteogenesis imperfecta, dwarfism, and *diseases of the nervous system*, such as Little's disease, anterior poliomyelitis, and subacute combined sclerosis due to pernicious anemia, are often accompanied by psychotic reactions, as stated by Lauretta Bender (Arch Neurol and Psychiat 32:1000 (Nov) 1934). The mechanism of the psychosis is due to (1) the discrepancy between the accepted normal bodily images and the body

structures as determined by the pathologic process; (2) the mysteriousness and obscurity of the disease which is not understood by the patient; (3) the thwarting of adult social, industrial and heterosexual adaptations, which are strivings which cannot be realized by the distorted body, (4) coincidental confusional or toxic symptoms that arise from the toxic features of the disease process or from pressure by distorted skulls on the brain and nerves, especially when deafness is involved.

These psychoses are characterized by 3 features (1) specific symptoms of imperfections of the body structure or discrepancy between the body image and body structure, (2) emotional upsets due to episodic or accumulative thwartings of the libido; (3) paranoid delusions, symptoms related to the feelings of mysteriousness of the pathologic process.

There is a definitely indicated therapeutic approach directed first at the somatic pathologic process, in an effort to alleviate the body distortion as much as possible and bring the body structure as near as possible to the normal image. The patient is entitled to as full an understanding of the pathologic process as can be made available, with acquaintance with others similarly diseased, and removal of the elements of mystery and obscurity. He should be aided to face and accept the disease and plan to adapt his life to give adequate libido satisfaction.

Mental symptoms are common in *pernicious anemia*, according to E. L. Hunt (New York State J Med 34 99 (Feb 1) 1934), some observers reporting their occurrence in 16 per cent of cases and others as high as 40 per cent. Mental changes are of 2 kinds, those which occur early in the disease and those which occur late. The *early symptoms* are apathy, indolence, abnormalities of conduct, and a lessening capacity for work. The *later symptoms* may resemble any type of psychosis from melancholia to mania, or dementia. The psychotic picture is not characteristic of the disease. Under proper pernicious anemia therapy the symptoms disappear, strengthening the viewpoint that they are of toxic origin. Some authors consider that the etiologic factors are cerebral lesions.

D. N. Parfitt (J Neurol and Psychopath 15 12 (July) 1934) reports 2 cases of psychoses associated with pernicious anemia, one in a woman, 33 years of age, who developed melancholia with confusional features. The mental symptoms disappeared under treatment with **liver extract**. The other case was a male, age 57, who developed a Korsakoff's syndrome during the course of pernicious anemia. Recovery followed the use of **liver extract** orally and subcutaneously.

H. E. Kiene (Rhode Island M J. 17:125 (Aug) 1934) reemphasizes the importance of thorough physical examination in patients showing psychotic symptoms. Recourse to consultations in the specialties to determine the advisability of correcting pathological conditions discovered and adequate laboratory analysis are urged. These methods are routinely followed at the psychopathic department of the Charles V. Chapin Hospital.

Three cases are reported in which physical illness appeared to be the etiologic factor in the production of the psychosis. The first case was that of a married woman who developed hallucinosis, delusions and excitability following the birth

of her second child, at which time there developed a *secondary anemia* as the result of blood loss. Complete mental recovery coincided with physical improvement. Several years later, at the age of 42, she became psychotic. Her mental symptoms were excitability, incoherence of thought and speech, disorientation and resistiveness. Physical and laboratory studies showed that the patient had a *prolapsus uteri* with secondary anemia. Recovery followed **vaginal hysterectomy** and **perineorrhaphy**. In this case the psychological effect of the uterine prolapse on the patient's life was considered an important factor.

The second case was that of a woman aged 42, who was admitted to the hospital because of hallucinations, confusion and rambling conversation. There was a history of hematemesis and blood in the stools about 5 months previously and again 3 months later. These symptoms returned 2 weeks prior to admission. A diagnosis of *duodenal ulcer* was made and satisfactory recovery followed the use of ulcer therapy.

In the third case, symptoms of depression with threats of suicide occurred in a woman aged 45, who had recently married and was fearful of coitus. Physical examination disclosed the presence of a *sclerosed hymen* and a *Bartholin's cyst* which made proper sexual relations impossible. An operation resulted in the patient being able to make an adequate marital adjustment. Although this patient was an unstable, poorly-adjusted individual who had been mentally retarded all of her life, psychotherapy alone would not have been successful without *surgical correction* of the gynecological pathology.





# OPHTHALMOLOGY

*by*

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**AMBLYOPIA.**—A case of amblyopia which developed several days after a hemorrhage from the uterus is reported by A. S. Barr (*Am. J. Ophth.* 17: 396 (May) 1934). There was marked loss of vision due to neuroretinitis and central scotomas in both eyes. Practically normal vision returned in one eye but very little improvement took place in the other. Four months later the fundi had a normal appearance but small central scotomas were present.

**BLINDNESS.—Prevention.**—The following measures are recommended by A. Fuchs (*Ibid.* 17: 232 (Mar.) 1934) for the prevention of blindness: (1) Prevention of gonorrheal conjunctivitis of the newborn by Credé's procedure; (2) the prevention of accidents by preventive measures; and (3) supervision of infectious diseases of the eye. He urges public enlightenment and instruction in hygienic measures, protection against ocular diseases and injuries, and in Egypt a campaign against flies. He believes flies are the germ carriers responsible for the enormous number of eye infections in Egypt.

**CHORIORETINITIS.**—Mettey and E. Redslob (*Ann. d'ocul.* 171: 396 (May) 1934) report a case of transudative pigmentary chorioretinitis in a young woman whose vision in the left eye had failed for 6 months. The macula was elevated, yellow-gray in color, and occupied an area of 2 disc diameters. The nerve head was swollen. Four years later vision was light perception. A neoplasm was suspected and enucleation was performed. Microscopic examination revealed degenerated retinal elements, dilated and thickened choroidal vessels, and patches of scar tissue obstructing one of the venæ vorticosæ. The obstruction produced the edema and the transudate which detached the retina.

**CONJUNCTIVA.—CONJUNCTIVITIS.—Diagnosis.**—The importance of the bacteriologic diagnosis of conjunctivitis for epidemiologic, diagnostic, prognostic and therapeutic purposes is stressed by P. Thygeson (*Arch Ophth.* 12: 676 (Nov.) 1934).

#### FILM TECHNIC.

Gram stain is used for conjunctivitis of bacterial origin, Giemsa stain is employed for trachoma and for inclusion conjunctivitis (inclusion blennorrhea and swimming-pool conjunctivitis), and for staining eosinophils in vernal catarrh.

Thygeson prefers the Hucker modification of Gram's stain, in which the following solutions are used:

#### *Ammonium Oxalate-Crystal Violet Solution.*

##### *Solution A—*

Crystal violet (85 per cent dye content)	4	Gm
Ethyl alcohol (95 per cent).	20	cc

##### *Solution B—*

Ammonium oxalate	0.8	Gm
Water	80	cc

Mix solutions A and B

#### *Compound Solution of Iodine*

Iodine	1	Gm
Potassium iodide	2	Gm
Water	300	cc

#### *Counterstain*

Safranin (saturated solution in 95 per cent alcohol)	10	cc
Water	100	cc

Stain the film for 1 minute with mixture of *A* and *B*. Wash in water. Immerse in the iodine solution for 1 minute. Wash in water, blot and dry. Decolorize by gently agitating the slide in 95 per cent alcohol for 30 seconds. Counterstain for 10 seconds. Then wash, dry and examine.

**Giemsa Stain.**—Dry the films in air for 5 minutes. Fix in chemically pure (acetone-free) methyl alcohol for 2 hours or longer. Transfer to a dilute Giemsa staining fluid (1 drop to 2 c.c. of neutral distilled water) and stain for 1 hour or longer. Decolorize for 5 seconds in each of 2 changes of 95 per cent ethyl alcohol. Dry in air.

For rapid diagnosis fix for 1 minute with the May-Greenwald stain. Dilute the fixative with an equal number of drops of neutral distilled water and allow the solution to remain on the film for 4 minutes. Transfer to a dilute Giemsa staining fluid and stain for 15 minutes or longer. Decolorize in alcohol. Dry in air.

**Method.**—Make 2 epithelial scrapings and 2 secretion films from each case. Place 1 epithelial scraping and 1 secretion smear in absolute methyl alcohol. Stain the secretion film by the Gram method. If it gives satisfactory information, discard the other slides.

#### CULTURE TECHNIC

**Mediums.**—Blood agar plates are used routinely.

**Method.**—Cultures are taken from the lower culdesac. In chronic blepharoconjunctivitis, cultures are also taken from the eyelid margins and the inner canthus. The cultures are incubated at 37° C.

Because early cases of *gonorrheal ophthalmia* cannot be distinguished clinically from the benign types of conjunctivitis, early diagnosis is important.

**Etiology.**—B. J. Powell, Jr. (*Am. J. Ophth.* 17:206 (Mar.) 1934) described unocular conjunctivitis from *peat dust*. This condition occurred in people who worked in a region subject to the irritating action of peat dust of a strongly acid nature combined with sharp spicules of silicon. This type of conjunctivitis is always unocular. It is due to the strong chemical action of the acid salts of the soil combined with mechanical erosion of the conjunctival epithelium from rubbing in the sharp silica spicules. He has found that the only treatment necessary is to overcome the spasm of the iris.

**Treatment.**—For *gonorrheal conjunctivitis*, P. Thygeson (*loc. cit.*) recommends intramuscular injection of **foreign protein** and the introduction of 0.5 per cent **silver nitrate ointment** into the conjunctival culdesac, for *pneumococcus conjunctivitis* 1 per cent **optochin**; for conjunctivitis due to *Koch-Weeks influenza bacillus* he prefers **silver nitrate ointment** (0.5 per cent) 4 times daily to the application of a solution of silver nitrate to the palpebral conjunctiva, in cases of pseudomembranous conjunctivitis a smear is important; for *diphtheritic infection*, **diphtheria antitoxin** locally and parenterally is advisable, for conjunctivitis caused by *hemolytic streptococci*, **scarlet fever antitoxin** has been advocated (H. C. Kleuver, *Chronic Streptococcic Pseudomembranous Conjunctivitis*, to be published).

Thygeson divides *chronic conjunctivitis* into 4 groups of cases: (1) those caused by the *diplobacillus of Morax*, (2) those caused by *Staphylococcus pyogenes aureus*, (3) those in which eosinophilic cells are found in the conjunctival secretion, and (4) those with negative findings. For Group (1) he recommends the continued use of **zinc sulphate ointment** for at least a month after the cessation of symptoms. For Group (2), **silver nitrate ointment** applied directly to the eyelid margins is useful. **Vaccines** are often effective.

No specific chemotherapeutic agent is known for Group (2). In Group (3) the presence of eosinophils may indicate vernal catarrh or simple conjunctival allergy. In Group (4) laboratory findings are of no assistance. He urges careful examination of the cornea with the slit lamp to exclude superficial punctate keratitis.

In cases of *trachoma* it is of assistance to determine whether the inflammatory signs are due to the action of the trachoma "virus" (P. Thygeson: Arch. Ophth. 12:307 (Sept.) 1934) itself or of superimposed bacterial infection. Laboratory findings may aid in determining whether treatment with **copper sulphate** or **silver nitrate** is indicated. Inclusion blennorrhea and swimming-pool conjunctivitis are not due to bacteria and are aggravated by the use of silver nitrate.

**OPHTHALMIA NEONATORUM.—Prophylaxis.**—The limitations of the use of silver nitrate in the prevention of ophthalmia neonatorum are discussed by L. Lehrfeld (M. Bull., Dept. Pub. Health, City of Philadelphia (Dec.) 1934).

There were 1437 cases of ophthalmia neonatorum reported in Philadelphia from 1918 to 1933, inclusive. These range from a very low peak of 56 cases in 1918 to a high peak of 137 in the year 1930, repeated in 1931, followed by a decrease of 67 cases in 1933. Of the cases reported from 1920 to 1933, 28 per cent were of the gonorrheal type and the remaining number nongonorrheal.

The survey shows that gonorrhea in pregnant women is not given the care and attention it deserves, particularly as a factor in the control of ophthalmia neonatorum. Too much reliance has been placed upon a single drop of a germicide in the eyes of the newborn, with full knowledge that the expectant mother has gonorrhea. In the past, too much stress has been placed upon the name of the germicide used, rather than upon the method of antisepsis of the eyes of the newborn and the control of the infection in the expectant mother.

The incidence rate of ophthalmia neonatorum in Philadelphia has not shown any appreciable decrease, primarily because the principles of antisepsis are not being followed out as laid down by Credé, *viz.*, **flushing the eyes** first, followed by instillation of **silver nitrate**.

**Sterilization of Birth Canal.**—It is interesting to note that in the 6 hospitals investigated, expectant mothers registered in the prenatal clinics are examined for the presence of venereal disease. In 2 institutions, when gonorrhea is found or suspected, there is observed a period of watchful waiting and dependence is placed entirely upon prophylaxis of the eyes of the newborn. In 2 other institutions all mothers whose smears are positive for the gonococcus, and those suspected of having gonorrhea, are placed under a régime of treatment during the last 2 months of pregnancy, aiming not to cure the gonorrhea, but to reduce the number of organisms present, or at least partially sterilize the birth canal so as to minimize, as far as humanly possible, infection of the newborn. Records show clearly that the 2 institutions which do not use prenatal antisepsis have 5 times the incidence rate of ophthalmia neonatorum shown by 2 hospitals which do use prenatal antisepsis.

Gonorrhea in pregnant women is greater in the negro race than in the white. This means that a great deal of attention in further reducing the incidence of

ophthalmia neonatorum should be centered around the control of gonorrhea in the colored race. This survey shows pointedly that mothers suspected of having gonorrhea may be so treated that they deliver babies free from any eye disease. It also shows that mothers who are not suspected of having gonorrhea and not treated prenatally may give birth to babies who actually have gonorrheal ophthalmia.

The author's deduction from these statistics is that all women in hospitals where there is a high incidence of gonorrheal infection should have systematic treatment, aiming toward partial sterilization of the birth canal prior to delivery, and cases should be followed up by the social service department after discharge from the hospital with the viewpoint of preventing secondary infections in the newborn weeks after birth.

A weak solution of **silver nitrate**—0.5 per cent—instilled after thorough flushing of the eyes with **boric acid solution**, would obviate that fear of inflammatory reaction commonly seen when using 1 per cent silver nitrate, and will obviate the prevailing fear of damage to the eyes by a stronger solution. In other words, the method and the germicide used should be such that the attending physician or nurse will have confidence in their effectiveness.

**OPHTHALMIA NEONATORUM, GONORRHEAL.**—C. E. Walker (Am. J. Ophth. 17:1146, 1934) examined 140 infants with ophthalmia neonatorum of gonorrheal origin to determine whether malnutrition had any bearing on the ulceration of the cornea. He found that ulcer of the cornea occurred more frequently in those patients who suffered from malnutrition. He recommends careful **dietary regulation** of patients with ophthalmia neonatorum as a supplement to the accepted local treatment.

A. F. MacCallan (Arch. Ophth. 12:819 (Dec.) 1934) discusses the rôle which the gonococcus plays in purulent ophthalmia. He concludes that although trachoma during the hot weather predisposes to infection by the gonococcus, pannus protects to some degree against ulceration of the cornea. The organisms which cause gonococcal urethritis are identical with those which produce gonorrheal conjunctivitis.

**Treatment.**—From a study of case records of 189 patients with gonorrheal ophthalmia, J. I. Farrell (Am. J. Ophth. 17:591 (July) 1934) concludes that the *prognosis* of a patient's gonorrheal ophthalmia is not dependent upon the presence or absence of a similar genital infection. These cases were treated at the Massachusetts Eye and Ear Infirmary from 1916 to 1931. Treatment consisted of 3 per cent **boric acid irrigations** followed by the instillation of 20 per cent **argyrol** and the introduction or application of **boric acid ointment**. Treatment was carried out at half-hour intervals. In cases with corneal involvement, 0.5 or 1 per cent **atropine sulphate**, 3 times a day, was instilled in the conjunctival sac. Of 189 cases investigated, 109 patients had had previous treatment or at the time of admission to the hospital, had a genital infection.

**PTERYGIUM.**—**Treatment.**—An operation has been devised by O. Edeskuty (Ztschr. f. Augenh. 83:109 (Apr.) 1934) which prevents the recurrence of a pterygium. In a pterygium the pathologic tissue is the subconjunctival proliferated connective tissue. By dissecting this tissue away from the

limbus to the region overlying the rectus muscle, no recurrence can take place. Edeskuty dissects the pterygium from the cornea, makes an incision at the limbus (2 mm. down from the horizontal meridian) and from each end of this incision makes a 12 mm. horizontal incision. He dissects all connective tissue from the posterior surface of this flap and from the underlying episclera and then replaces the flap and sutures it back into place above and below.

**STAPHYLOCOCCI.**—According to G. H. Gowen (Am. J. Ophth. 17: 36 (Jan.) 1934), the skin of the lower eyelid is the source of contamination of the conjunctiva. Staphylococci are constantly transferred from it to the lower eyelashes by the overlapping of the upper eyelash in winking, and thence to the conjunctiva. Transmission by way of the nasolacrimal passage is excluded.

He found that patients who have staphylococcus aureus or citreus on the skin around the eye also have this organism in the conjunctiva; those who have only staphylococcus albus on the skin have only the albus type in the conjunctiva. The skin of the upper eyelids does not serve as a source of contamination to the upper eyelashes. The skin of the lower eyelid is a constant source of contamination to the lower eyelashes. It is interesting to note that when the organisms disappear from the lower eyelashes, conjunctival contamination ceases.

**TRACHOMA.**—*Etiology.*—Schousboë (Rev. internat. du trachome 11: 19 (Jan.) 1934) concludes from his study of trachoma in infants that the infection occurs in the first few months of life (45 per cent. at 24 months). It is transmitted to the infant by the mother or by the members of the immediate family.

*Pathology.*—Gross or biomicroscopic signs of pannus are uniformly present in all stages of trachoma, according to P. Thygeson (Am. J. Ophth. 17: 787 (Sept.) 1934). His conclusion is based on a biomicroscopic study of the limbus corneæ in 31 cases of trachoma and in a number of other conjunctival diseases.

1. In cases of *early trachoma* the vascular and infiltrative changes at the limbus serve to differentiate trachoma from follicular conjunctivitis. With the slit lamp incipient pannus is seen to consist of a widening of the zone of end-capillary loops with extension of the loops into the cornea. A diffuse or punctate superficial infiltration usually precedes the vessels.

2. In cases of *advanced trachoma* vascularization involves the entire circumference of the cornea, is regular, most pronounced above, and the infiltration extends beyond the vessels.

3. In cases of *healed trachoma* characteristic and uniformly arranged vascular changes always remain at the limbus and in the cornea.

*Diagnosis.*—The diagnostic signs of trachoma are listed in the following order by A. F. MacCallan (Rev. internat. du trachome 11: 38 (Jan.) 1934):

(1) Follicles on the upper tarsal conjunctiva; (2) a papillary overgrowth sometimes masking the follicles; (3) pannus; (4) follicles at the limbus, called Herbert's rosettes, or their cicatricial remains, called Herbert's peripheral pits; (5) cicatrices on the upper tarsal conjunctiva; (6) permanent thickening of the fibrous tissue of the upper eyelid; (7) pseudoptosis; (8) a sinuous appearance

of the border of the upper eyelid; (9) post-trachomatous degenerations, consisting of small cysts filled with inspissated material; (10) facets of the cornea; (11) epithelial plaques of conjunctiva and cornea; (12) infiltrations of the cornea; (13) trichiasis; and (14) entropion. Pannus accompanied by any of these diagnostic signs is pathognomonic of trachoma.

**Treatment.**—C. Trapesontzewa and Z. Nikolskaja (*Ibid* 11:29 (Jan) 1934) have found that chaulmoogra oil has a bactericidal action on some bacteria and molds, particularly on the bacilli of tuberculosis, diphtheria and leprosy. They have found that the combination of **chaulmoogra oil with copper** is effective in the treatment of trachoma.

I Wasserman (*Sovet vestnik oftal* 3 399, 1933) advocates **repeated gentle expression of the follicles** in trachoma under local anesthesia every 4 to 5 weeks. He reports complete cure in 91 of 107 cases. In his series of cases the average number of expressions was 4. A **solution of zinc sulphate** (0.25 per cent) is instilled into the conjunctiva by the patient.

F. Pervoochin and G. Kalnikov (*Ibid* 4 444, 1934) conclude that **x-ray therapy** is valuable in the treatment of trachoma. After 5 or 6 treatments with 30 to 40 per cent of the erythema dose at 1 to 3 weeks' interval, 26 patients showed marked improvement.

Favorable effects have been obtained by F. Motais (*Rev. internat. du trachome* 11 65 (Apr) 1934) in trachoma, with or without entropion through **tarsectomy** by the cutaneous method of approach. The operation corrects entropion and trichiasis, and has a quieting influence on the main disease, probably because of the removal of infected glands in the tarsus. He recommends this procedure for all cases of cicatricial or granulocicatricial trachoma which have thickened tarsus and symptoms of irritation.

In 3 cases of **Denig's operation** for trachoma reported by A. Z. Mishulina (*Sovet vestnik oftal* 4 498, 1934) it became necessary to excise the transplant because inflammatory changes had taken place in it. In Denig's operation, mucous membrane taken from the lips or mouth is transplanted at the upper limbus of the cornea to prevent the progressing pannus. Microscopic examination revealed that the transplant had assumed the characteristics of the ocular conjunctiva and had become involved in the trachomatous process.

**VERNAL CATARRH.—Treatment.**—The results obtained by Dedimos (*Arch. d'opht.* 51 277 (May) 1934) in the treatment of vernal catarrh by subconjunctival injections of **adrenalin** are reported. Of 15 patients, 7 were cured, 4 improved and 3 were unaffected by the treatment. The method was introduced by Tessier. An initial dose of 0.2 c.c. (3 minims) increased progressively to 0.5 c.c. (8 minims) of a solution of 1:2000 adrenalin is injected as close to the lesion as possible. Twelve to 15 doses are given at intervals of 2 days. The courses may be repeated. Results were better in the bulbar type of case but some of the palpebral type accompanied by granulations improved after a second course of treatment 15 days after the first course. He believes vernal catarrh results from irritation by sunlight in individuals who are of a vagotonic nature or who have disturbances of the sympathetic nervous system.



**CORNEA.—CONICAL CORNEA.**—A case of conical cornea complicated by acute ectasia is reported by G. E. Berner (Am. J. Ophth. 17:22 (Jan.) 1934). Acute ectasia occurred in the left eye of a young girl who had bilateral keratoconus. Examination with the slit lamp revealed that the ectasia was due to infiltration of fluid into the spaces of the substantia propria of the cornea. Repeated **paracentesis** and the daily application of a 1 per cent. solution of **formalin** to the apex of the cone reduced the ectasia and the opacity. With **contact lenses** vision was improved to 6/9.

**DYSTROPHY.**—A case of dystrophy of the endothelium of the cornea is described by E. L. Goar (*Ibid.* 17:215 (Mar.) 1934). He found this condition in about 6 per cent. of people above 20 years of age. The dystrophy usually begins in the fourth or fifth decade and is 3 times as common in women as in men. It is a chronic disease of the endothelium of the cornea characterized by irregular thickenings and excrescences of Descemet's membrane.

**CORNEAL GRAFTS.**—E. Galante (Ann di Ottal. e. clin. ocul. 62:119 (Feb.) 1934) reports the results of his experiments with corneal grafts. He took the corneal tissues from the eyes of 6 dogs and inserted them in the eyes of 6 rabbits and *vice versa*. The grafts regained their sensibility and retained their transparency.

**KERATITIS.**—In a case of calcification of the cornea (*band-shaped keratitis*) with changes in the conjunctiva in a boy 18 years of age, reported by F. B. Walsh and E. Chan (Am. J. Ophth. 17:238 (Mar.) 1934), the thickened conjunctiva extended down upon the cornea from above in the form of finger-like processes which overlapped the corneal margin. Band-shaped keratitis may be primary, due to a nutritional defect of the cornea, or secondary, following chronic inflammation of the eye, *e.g.* iridocyclitis.

R. J. Sisson (*Ibid.* 17:222 (Mar.) 1934) examined the opaque substance which forms as a band in the interpalpebral area of the cornea in *band-shaped keratitis*. By the use of x-ray spectra and microscopes with polarized light, he proved the presence of calcium, phosphorus, sulphur and silicon. *Treatment* consists in the **removal of the opaque material** by scraping it with a sharp spud. The nutrition of the eye seems to improve after the ingestion of **fruit juices** and the performance of an **iridectomy**.

A case of primary *keratitis bullosa* is reported by W. T. Davis (*Ibid.* 17:24 (Jan.) 1934) which responded well to **x-ray** treatment after the usual medical and surgical treatment had failed. Keratitis bullosa is characterized by recurrent large blebs. The blebs rupture and leave ulcerated areas, which result in scarring of the cornea with impairment of vision or destruction of the eye. Bullous keratitis may be (1) primary, occurring spontaneously with no history of trauma, or (2) secondary (*a*) traumatic, resulting from abrasion of the corneal epithelium or as a sequel to intraocular foreign body, (*b*) associated with glaucoma or iridocyclitis; (*c*) dystrophic, as in pannus degenerativus of Fuchs.

Keratitis bullosa runs a chronic course with recurrent attacks of severe pain for many years. Vision is impaired and the intraocular pressure usually becomes elevated.

*Treatment* is as follows Relief of the symptoms, removal of the bleb, and prevention of its recurrence and of its complications. **Holocaine, dionin, atropine, pressure bandage with pilocarpine** or with **iridectomy**, and the application of **tincture of iodine, silver nitrate** or the **galvanocautery** to the base of the bleb after its **removal**.

In this case 13 treatments with x-rays were given over a period of 6 months, as follows 5 milliamperes, 140 kilovolts, 10-inch distance, 5 millimeters aluminum filter, time of exposure  $2\frac{1}{2}$  minutes. This is equal to 90 international r units or about  $\frac{1}{3}$  of the amount required to produce a mild erythema of the skin. The skin was protected by a lead shield and the eyelids were kept open.

M. Dvorschetz (Sovet. vestnik oftal. 4:395, 1934) believes that the virus of *influenza* causes the ocular complications of "grippe" A *phlyctenular keratitis* which was indistinguishable from the phlyctenular keratitis of children occurred in adults between the ages of 20 and 60 years *Parenchymatous keratitis* of "grippe" was always unilateral Its course was milder and of shorter duration than that of syphilitic or tuberculous keratitis.

The diagnosis and treatment of *tuberculous parenchymatous keratitis* are discussed by A. Moreu and A. Prior (Arch. de oftal. hispan. am. 34:1 (Jan.) 1934) After acquired or congenital syphilis has been ruled out, diagnosis is based on the presence of tuberculous stigmas, positive local and general tuberculin reactions, involvement of uvea and sclera, angiopathies of the retina, yellow-white infiltrates around nodules in the cornea with involvement of the endothelium and affection of one eye They report 12 cases of tuberculous keratitis and recommend the following treatment **phototherapy, liver therapy**, and the intramuscular and subconjunctival injection of **gold salts**.

**LEUKOMA.—Treatment.**—W. L. Benedict (Arch. Ophth. 11:32 (Jan.) 1934) reports that he obtained not only a cosmetic result but also slight improvement in vision in a few suitable cases of leukoma of the cornea by **excision of the anterior layers of the cornea**. He recommends **resection** of a large quadrilateral area of the cornea His report is based on results obtained in 17 cases of congenital and acquired leukoma of the cornea.

*Keratoplasty*—R. Castroviejo (Am. J. Ophth. 17:932 (Oct.) 1934) reports the results he obtained in 7 cases of keratoplasty With his own technique and with specially designed instruments he performed partial penetrating keratoplasty on an unselected group of patients The most suitable eyes for this operation are those in which there is a moderately dense leukoma with portions of clear cornea contiguous to the intended graft, and in which the leukoma is the only pathologic condition present.

The transplant should be taken from an enucleated eye, the cornea of which is entirely clear It should not be taken from a glaucomatous eye The donor should preferably be young.

There are 3 methods of corneal transplantation total, partial superficial, and partial penetrating, the last offers the best permanent results. The transplant may be obtained from the same individual (autoplasty), or from individuals of the same species (homoplasty). Heterotransplants invariably become opaque.

Anterior and posterior transillumination is of assistance in examining eyes with dense leukomas which involve the entire corneal area.

Castroviejo's technic is as follows:

Obtain a rectangular graft, 4 mm. square, corresponding exactly in size to the opening in the cornea of the recipient; bevel the edges in both the transplant and in the cornea of the recipient's eye so that the anterior surface of the graft is larger than its posterior surface; make conjunctival flaps to hold the transplant in position by gentle uniform pressure. The flap of conjunctiva accelerates the process of healing, furnishes the necessary nutrition while cicatrization takes place during the first few days, makes a water-tight union which favors the prompt restoration of the anterior chamber, and protects the graft and the eye in case the former becomes partially detached or does not heal.

H. L. Hilgartner and H. L. Hilgartner, Jr. (Arch. Phys. Therapy 15:103 (Feb.) 1934) have found **radium** of value in the treatment of trachoma, corneal opacities, leukoma and recurrent pterygia. For leukomas of the cornea they advise **excision of the scar tissue** followed by repeated exposure to 10 mg. of **radium** for from 3 to 5 minutes.

**OPERATIONS.—Delimiting Keratotomy.**—In order to arrest progressive-suppurative disease of the cornea, H. S. Gradle and S. R. Gifford (Am. J. Ophth. 17:602 (July) 1934) advocate a delimiting keratotomy in which the incision passes through the cornea tangential to the progressing border of the ulcer. The improvement is due to the resulting hypotony and increase in the number of antibodies and the nutritional elements. When ulcerative keratitis fails to respond to the usual treatment delimiting keratotomy is indicated.

**TATTOOING.**—T. Sapir (Sovet vestnik oftal 4:41, 1934) has obtained satisfactory results in 290 cases of opacities of the cornea by tattooing the cornea with **gold chloride**. The chief danger of this method is that it may set up a severe inflammation in an eye which has been quiet for many years.

**ULCERS.—Treatment.**—A new method for the treatment of corneal ulcers has been devised by E. Klauber (Ann. d'ocul. 171:424 (May) 1934). He surrounds the edge of advancing ulcers with an area of **tattooing**. For tattooing he uses **gold chloride** and **tannic acid**.

The early use of the **electrocautery** in the treatment of ulcers of the cornea is strongly recommended by A. W. Morse (Am. J. Ophth. 17:608 (July) 1934). He finds that it controls the infection, allays pain, shortens disability and prevents further loss of vision. Healing takes place in a few days, with slight scarring.

For *small and superficial ulcers*, the cautery point should be heated to a cherry-red color, or even a little beyond this color to yellow. The cautery radiates heat and sterilizes small superficial ulcers by being brought very close to them, without making actual contact. This was suggested by D. W. Green (Wood's "A System of Ophthalmic Therapeutics," p. 81, Cleveland Press, Chicago, 1909).

For *deeper and larger ulcers*, actual contact is necessary. The cautery point is brought only to a dull red heat, or even to practically no color, and tested on a piece of cotton to prove that it is actually hot. The point is applied to the

edge of the ulcer and quickly withdrawn. This procedure is repeated until the ulcer has been completely cauterized by applications 2 mm apart

For *large ulcers*, the progressing part of the ulcer is touched once or twice with the cautery at low heat to sterilize the edge of the ulcer and to penetrate to the depth of the infection. To sterilize the more superficial part of the ulcer the cautery point is made hotter, and brought close, but not in contact with the ulcer

For a *progressing ulcer* which undermines normal cornea at the edge, he advises cauterization through the superficial normal cornea to reach the advancing infection. One application of the cautery usually checks the progress of the ulcer but if the areas are still progressing, treatment may be repeated as often as necessary

T Barg (Sovet vestnik oftal 4 73, 1934) has employed **carbolic acid crystals** in 7 cases of serpiginous ulcers of the cornea. He finds that **cauterization** has a bactericidal effect, hastens healing, and relieves pain.

**EYE. — DIAGNOSIS. — Tuberculin.** — It has been concluded by G Márquez and J Soriano (Klin Monatsbl f Augenh 92 628 (May) 1934) that the Calmette reaction is not only harmless but it is diagnostic. All patients with tuberculosis react positively to less than 1 per cent of tuberculin or even to extremely weak solutions. Normal subjects do not react to weak solutions and may require at least a 1 per cent solution to produce a slight reaction. The subcutaneous injection of 1 mg of tuberculin to bring about a focal reaction is a dangerous procedure

**EPINEPHRINE.—Action on Normal Eye.**—S C Howell (Arch Ophth 12 833 (Dec) 1934) reports the results of his experiments to determine the action of epinephrine on the normal eye. He finds that (1) in susceptible individuals systemic absorption of epinephrine from the ocular conjunctiva may give rise to a general reaction. (2) Instillation of a 2 per cent solution of epinephrine into the conjunctival sac of the normal eye usually lowers the intraocular tension within 1 hour. A similar but less marked reduction in tension may occur in the opposite eye. (3) Dilatation of the pupil occurs within 1 hour and may last 24 hours without increasing the intraocular tension. Epinephrine is a harmless mydriatic which may be used to facilitate the study of media and fundi of eyes in which atropine or its derivatives might be harmful

**MENINGIOMAS.**—Two cases of intracranial tumors which were attached to the most mesial part of the sphenoid ridge are reported by C A Elsberg and C. G. Dyke (*Ibid* 12 644 (Nov) 1934). Tumors in this situation produce a characteristic syndrome, *viz*, unilateral atrophy of the optic nerve with a defect of the visual field on the same side. Slight changes of the sella turcica and alterations in the shape of the interpeduncular cistern are revealed by x-ray. They urge early recognition of this syndrome and removal of the tumor while it is small

**NASAL NERVE SYNDROME.**—J. M. V. Ortiz (Ann d'ocul 171 479 (June) 1934) reports a case of nasal nerve syndrome which presents a new clinical form. The condition occurred in a young woman 27 years of age. She

complained of severe attacks of pain in the region of the left orbit. The pain radiated toward the ala of the nose and the parietotemporal area of the head. Pain was accompanied by photophobia, epiphora and excessive nasal discharge on the same side. The symptoms disappeared after the application of **cocaine powder** and **epinephrine solution** to the anterior part of the left nasal cavity. There was no lesion of the cornea or iris. The syndrome may be produced by local causes (nasal spur, deviated septum) or by remote causes (syphilis, diabetes, dental caries)

**SYPHILIS.—Treatment.**—Following an examination of 87 patients with neurosyphilis who were undergoing tryparsamide therapy, L. L. Mayer and R. D. Smith (Illinois M. J. 65: 258 (Mar.) 1934) conclude that **tryparsamide** does not produce optic atrophy in cases where syphilis has not already damaged the nerve and that tryparsamide does not aggravate a previously existing atrophy produced by syphilis.

E. D. Osborne (Am J Ophth. 17: 537 (June) 1934) suggests the following treatment for ocular syphilis (1) Cases of *early syphilis* of the eye improve promptly under combined **arsphenamine** and **bismuth therapy**. The manifestations of early syphilis are chancre of the eyelids and conjunctivæ, mucous patches of the conjunctivæ, iritis and syphilitic involvement of the uveal tract.

2 *Late syphilis* of the eye should be treated with combined **arsphenamine** and **bismuth therapy** at intervals of approximately 4 months between courses of arsphenamine with bismuth during the interim. Late syphilis includes iritis, iridocyclitis, choroiditis, retinitis, neuritis and interstitial keratitis of acquired syphilis. The last condition is not nearly so rare as many authors have stated. He has seen 3 cases in the past year. This condition is important from the standpoint of workmen's compensation. Interstitial keratitis from acquired syphilis usually responds to antisiphilic treatment more rapidly than the congenital form. Any resistant case of late syphilis should be subjected to **fever therapy** without hesitation.

3 *Congenital syphilis* of the eye. This group includes interstitial keratitis and the same conditions mentioned in Group 2. During the past 8 years every case of interstitial keratitis has improved after the combined use of **sulpharsphenamine** and **bismuth** intramuscularly, with repeated courses of **arsphenamine**. Treatment should be combined and carried to the limit of tolerance. **Fever therapy**, either in the form of malaria or produced by the split dose method of typhoid vaccine intravenously, materially shortens the duration of the attack. Persistent, continuous treatment has prevented recurrence and the involvement of normal eyes.

4 *Neurosyphilis* with eye manifestations. This group includes optic atrophy, neuritis, and retinitis. Patients with these conditions were given one strenuous course of combined **arsphenamine** and **bismuth** followed by **fever therapy**. The results were incomparably better than with arsphenamine or bismuth alone or combined with Swift-Ellis intraspinal therapy.

**TREATMENT OF EYE DISEASES.—Vaccine fever therapy** was employed by A. Batignani (Lettura Oftal. 11: 141, 1934) in 75 cases of ocular diseases. These included keratohypopyon, phlegmonous dacryocystitis with peri-

ostitis, trachoma with corneal complications, perforating injuries, vitreous hemorrhage, and syphilitic parenchymatous keratitis. Large doses of **antipyogenic vaccine** were given intravenously. The febrile reaction and leukocytosis were responsible for the improvement. This treatment is contraindicated in patients with cardiac or renal disease.

A. Ferrari (Arch. di ottal. 41:127 (Mar) 1934) has used 2 c.c. ( $\frac{1}{2}$  dram) of **colloidal sulphur** injected intramuscularly every 2 or 3 days in nonsyphilitic eye diseases. Injections were followed by a considerable rise in temperature and improvement in the condition of ulcers of the cornea, parenchymatous keratitis, uveitis, iridocyclitis after cataract extraction, septic wounds of the cornea with hypopyon, and in 2 cases of optic atrophy.

J. Majoras (Klin. Monatsbl. f. Augenh. 93:81 (July) 1934) substituted **posterior pituitary hormone (meropitan)** as a local anesthetic in patients who develop cardiac palpitation, tremor, and a sense of oppression from adrenaline. Meropitan produces a slower, slighter but more lasting rise in blood-pressure. The blood sugar is not increased. Two years of satisfactory clinical experience with meropitan has led him to adopt it in eye operations.

P. C. Jameson (Arch. Ophth. 12:635 (Nov) 1934) has found that a solution of **thyroxin**, when instilled into the conjunctival sac, is of value in certain eye conditions. By instilling a solution containing 1 mg. ( $\frac{1}{65}$  gram) of thyroxin to 1 c.c. (16 minims) as often as twice a day, he obtained improvement in the following conditions: lenticular opacities, keratitis, kerato-iritis, corneal opacities, iritis and vitreous opacities. He believes that his clinical results are sufficiently satisfactory to establish thyroxin as a local metabolic stimulant and alterative.

J. N. Duggan and B. P. Nanavati (Bull. Ophth. Soc. Egypt, 26:221, 1933) have treated external diseases of the eye with **ultraviolet light** from the Birch-Hirschfeld carbon arc lamp. Ultraviolet light is effective in hypopyon ulcers, episcleritis, phlyctenular conjunctivitis and keratitis.

**TUBERCULOSIS—Treatment.**—Twenty cases of tuberculous iridocyclitis of the anterior segment of the eye were treated by A. Garcia Miranda (Arch. de oftal. hispano-Am. 34:349 (July) 1934) by **intraocular autohemotherapy**. About 0.1 c.c. ( $1\frac{1}{2}$  minims) of blood is injected into the anterior chamber after withdrawal of the aqueous. Blood is taken from the patient's arm. The inflammatory symptoms disappeared rapidly and vision improved considerably. In 17 cases only 1 injection was necessary, in 1 case, 4 injections, in 2 cases, 2 injections.

**SPECIFIC TREATMENT—A-O—B.** Nakamura (Arch. Ophth. 10:161 (Aug) 1933). Before the time of A. von Hippel, who founded the so-called second tuberculin era in ophthalmology, tuberculins usually were used in large doses for the treatment of ophthalmic tuberculosis. Uhthoff (1891) gave 0.5 mg. of old tuberculin to children and 1 mg. to adults. Königshofer and Maschke (1891), Schwaer (1891), and Cohn (1891) gave 0.75 mg. Diem (1906) gave from 1 to 3 mg. and Schaffranek (1909) gave 1 mg. Other ophthalmologists have administered even larger doses. In most of the cases, however, this mode of application of tuberculin did not bring about the anticipated success, but, on the

contrary, proved to be injurious, as it produced anaphylactic symptoms which were peculiar to the nature of tuberculous diseases.

Since the time of von Hippel and his pupil, Schieck, the views and principles of tuberculin treatment of patients with tuberculous ophthalmic diseases have changed somewhat, von Hippel contending that strong focal and general reactions should be avoided under all circumstances. Much smaller doses were therefore used in beginning treatment. Thus, von Hippel (1914) and Werdenberg (1925) used 0.1 c.c. of a 1:1,000,000 dilution of old tuberculin as a commencing dose. It stands to reason that the final dose was likewise very much lower in comparison with that of former times.

The treatment of ophthalmic tuberculosis with tuberculin for the past 20 years may be divided into the following 6 periods: In the *first period* (1910-1913) a mixed tuberculin (old tuberculin, 1 part; new tuberculin (TR), 3 parts; and emulsion of bacilli (BE), 6 parts) was used—a 1:10,000 dilution administered every fourth day, in increasing doses, beginning with 0.1 c.c.; in the *second period* (1913 to 1915), emulsion of bacilli (BE), in increasing doses, commencing with from 0.01 to 0.1 mg. every fourth day; in the *third period* (1915-1918), emulsion of bacilli (BE), in increasing doses, commencing with 0.001 mg. every fourth day; and in the *fourth period* (1918 to 1920), emulsion of bacilli (BE), in increasing doses, commencing with 0.0001 mg., every fourth day.

The greatest success was obtained in the first period. Eighty per cent of the patients progressed favorably. But, in all 4 periods treatment had to be stopped on account of the allergic reaction when increased doses were used. Further treatment with tuberculin often became impossible. Therefore, in the *fifth period* (1921 to 1925) 0.1 c.c. of a 1:100,000 dilution of emulsion of bacilli (BE) was used without increasing the dose in the further course of treatment. The degree of success at this time was nearly twice that in the fourth period, in which the results were unfavorable owing to the too rapid increase in the dose. In the *sixth period* (from 1926) A-O, a new tuberculous vaccine discovered by Arima and Aoyama was used exclusively. One c.c. of A-O No. 1 (the smallest dose for adults) administered once a week nearly always brings about a subsidence of the disease without any unfavorable reaction.

The point to be stressed is the question of increasing the dose of tuberculin during treatment. This practice which is followed in most hospitals at present, seems useless. When von Hippel was using increased doses, he frequently had to stop treatment on account of a change in the symptoms for the worse, and postpone further injections until the irritation had subsided. The aggravation of ophthalmic tuberculosis caused by tuberculin often makes further specific therapy impossible.

The effects of an actively immunizing therapy on ophthalmic tuberculosis may be divided into 3 groups. A curative reaction without symptoms of irritation; a curative reaction with preceding symptoms of irritation; and an aggravation, *i. e.*, symptoms of an intensive irritation without a subsequent curative reaction. Only in this way can it be understood how Arima and his coworkers succeeded in obtaining a measurement of the immunizing value of A-O. Accord-

ing to Arima, only the "optimum dose" is able to bring about the cure of the tuberculous disease in the animal without an unfavorable result, whereas the larger doses not only produce no curative effect, but even tend to bring about an aggravation of the ophthalmic disease and generalization of the tuberculous process.

The irritation of the tuberculous focus produced by tuberculin, which formerly was erroneously thought to be favorable, is therefore not only useless, but harmful. When the optimum dose has been determined, either by clinical experience or by scientific experiments, it is advisable, therefore, to maintain this dose. By using the optimum dose, the problem of the specific treatment of ophthalmic tuberculosis is solved once and for all time.

With respect to the use of tuberculin in the treatment of recurring phlyctenæ, the only reference found in the literature was that Schieck used 0.2 c.c. of a 1:100,000 dilution of tuberculin from 2 to 3 times a week without increasing the dose. It is believed that ophthalmologists should extend the use of the optimum dose not only to the treatment of phlyctenæ, but also to the tuberculous diseases of the eye. In the fifth period (1921 to 1925) tuberculin (BE), in the same optimum dose, was used and favorable results were obtained. As mentioned before, since 1926 only A-O in the smallest dose has been used. In all forms of ophthalmic tuberculosis A-O has proved to be the best remedy as compared with other tuberculins. Eighty-four per cent. of the patients treated from 1926 to 1930 showed a favorable result. A-O cured *exudative uveitis* and so-called *sympathetic ophthalmia*, on which the usual therapy and tuberculin had no influence. In all, 1288 patients were treated at the Ophthalmic Infirmary of the Osaka Imperial University from 1926 to 1932. However, the results in 785 of these cases must be eliminated as unreliable, as the patients did not undergo the necessary observation. Of the remaining 503 cases in which accurate observations were made, in 89.5 per cent. the conditions subsided and in 10.5 per cent. they remained unchanged. In this latter series the following diseases were noted: Retinitis centralis, retinitis stellata, retinitis exudativa, retinitis diffusa, amotio retinae, retinitis proliferans, retinitis tuberculosa, neuroretinitis, retinal hemorrhage, hemorrhage into the retina and the vitreous humor, hemorrhage into the vitreous humor, opacity of the vitreous humor, neuritis optica, choked disc, atrophy of the optic nerve, neuritis retrobulbaris, choroiditis diffusa acuta, chorioretinitis, choroiditis of long-standing, iritis serosa, iritis fibrinosa, iritis sero-fibrinosa, iritis of long-standing, iritis tuberculosa, uveitis, cyclitis serosa, iridocyclitis, sympathetic ophthalmia, solitary tubercles of the choroid, tubercles of the episclera, scleritis, scleritis with episcleritis, keratoconjunctivitis eczematosa, keratitis eczematosa, keratitis fasciculosa, infiltratio corneæ, marginal vesicles, keratitis parenchymatosa, injuries of the cornea, conjunctivitis tuberculosa, paralysis of the muscles of the eye, ophthalmoplegia interna, and other conditions. These conditions were tuberculous, were suspected of being tuberculous, were not certain etiologically or defied antisyphilitic treatment. The great advantage of A-O is that, used in nonincreasing doses, it never creates unfavorable results, but has only a curative effect on the disease.



**EYEBALL.—BUPHTHALMOS.—Treatment.**—S. R. Gifford (Arch. Ophth 11.751 (May) 1934) recommends **iridencleisis** for buphthalmos. He performed this operation in 5 eyes and obtained complete success in 3 eyes. After iridencleisis was repeated, normal tension was obtained in the fourth eye. In the fifth eye normal tension was maintained but the vision failed after 2 years. His method is a modification of Holth's technic.

Two cases of buphthalmos in siblings are reported by C. Hymes (Am. J. Ophth. 17:132 (Feb.) 1934). The condition occurred in sisters. Excellent surgical results were obtained in both cases by the **Elliot trephining operation**. In the elder child operation was done on one eye when the child was 16 months of age and on the other eye at 3 years of age. One eye was lost and vision in the other was 5/200. The younger child was operated on at 9 months of age with conservation of useful vision. Buphthalmos is a congenital and hereditary disease characterized by increased intraocular pressure and stretching of the sclera and cornea of the infant, resulting in enormous enlargement of the cornea. Hymes urges the earliest possible surgical intervention in such conditions. Best results are obtained when the child is operated on before the age of 1 year.

**ENOPHTHALMOS.—Horner's Syndrome.**—According to H. P. Wagener (*Ibid* 17 209 (Mar) 1934), enophthalmos is rarely present in Horner's syndrome (paralysis of the cervical sympathetic nerve). Readings taken with the exophthalmometer in 94 of these cases showed enophthalmos in only 1 case. A comparison of average readings in patients with Horner's syndrome with those from 2 groups of the same number of normal subjects indicated a tendency to enophthalmos in those affected with this syndrome. He attributed enophthalmos to shrinking of the tissues of the orbit which results from loss of the trophic influence of the cervical sympathetic nerve. He does not believe that enophthalmos is due to relaxation of the smooth muscles of the eyelids and orbits.

Horner's syndrome is characterized by ptosis, miosis and enophthalmos. In this series pressure from nodes or tumors in the cervical region was the most common cause of the syndrome. Wagener points out that a difference of more than 2 mm. in the position of the eye should be present before one eye is considered enophthalmic or exophthalmic. Enophthalmos in man did not follow after cervicothoracic sympathetic ganglionectomy had been performed for the relief of Raynaud's disease of the upper extremities.

**EXOPHTHALMOS, PULSATING.—Treatment.**—The physiologic considerations in the treatment of pulsating exophthalmos are discussed by G. M. Dorrance and P. E. Loudenslager (*Ibid* 17 1099, 1934). They conclude as follows. Ligation of the proximal artery (the internal carotid) produces a reflux of blood from the artery distal to the fistula. This reflux may keep the fistula active and possibly produce cerebral complications. Ligation of the common artery, on the other hand, is really only a partial ligation of the internal carotid artery. Because of reversal of flow in the external carotid artery the internal carotid becomes a branch of the external with about 50 per cent reduction in volume flow. The partial reduction in blood-pressure in the internal carotid is then insufficient to start a backflow from the distal artery. Therefore,

the vessel will shrink in size, its lumen will be narrowed, and the size of any fistula present will thereby be reduced.

**GLAUCOMA.**—It is pointed out by E. Kraupa (*Ztschr. f. Augenh.* 84:43 (Aug.) 1934) that increased intraocular tension is not an unusual sequel to syphilitic keratitis. It may disappear after paracentesis of the anterior chamber or even without treatment. He reports 3 cases in which increased tension appeared many years after the keratitis had healed. Since medical treatment proved useless in these cases, he performed an **iridectomy**, an **Elliot trephine** and a **cyclodialysis**. If the tension still remained high, he repeated the cyclodialysis. Damage of the endothelium of the cornea may be a local cause of the glaucoma.

R. L. Raymond (*Brit. M. J.* 1:102 (Jan. 20) 1934) directs attention to increased intraocular tension in young persons as a cause of severe frontal headaches. He reports 4 cases in men between the ages of 25 and 30 years. Cupping of the discs was seen in only 1 case. Vision was not affected. Headaches were relieved by the instillation of **eserine** into the conjunctival sac.

**Diagnosis.**—R. I. Lloyd (*Am. J. Ophth.* 17:579 (July) 1934) points out (1) that for the early detection of the typical scotoma of simple glaucoma it is important to use test objects with a small visual angle against a flat surface, (2) that examination of the fields with the perimeter has its limitations, and (3) that field studies are the only reliable indicators of gain or loss.

In glaucoma cases the mapping of field defects before and after the use of miotics often reveals the disposition of the individual case. For prognostic purposes it is important to note the outline of the field and the defect extending from the blind spot, passing above and below the macular area.

**Treatment.**—In 11 cases of glaucoma L. T. Post (*Arch. Ophth.* 11:187 (Jan.) 1934) used **levoglaucozan** and **epinephrine bitartrate** in the non-surgical treatment of chronic simple glaucoma. Acute and secondary glaucoma are not benefited by these drugs.

L. K. Soloviev (*Sovet. vestnik oftal.* 5:21, 1934) recommends **posterior sclerectomy** as a substitute for enucleation in painful absolute glaucoma. He performs a trephine in the region of the equator and repeats the operation several times if necessary.

**GLAUCOMA, INFANTILE.—Pathogenesis.**—J. F. Hardesty (*Am. J. Ophth.* 17:689 (Aug.) 1934) suggests that it is possible that a relationship exists between hyperactivity of the thymus and infantile glaucoma. This suggestion is based on his findings in 29 cases of infantile glaucoma and in 3 of Magitot's. One patient, 6 months of age, had an enlarged thymus and blood calcium at the upper normal limit. The eyes improved as the size of the thymus diminished under x-ray therapy. The other patient, 1 year of age, had symptoms of hyperactivity of the thymus, suggesting vagotonia and hypofunction of the adrenals, although the thymus was not enlarged. The blood calcium in this case was just above normal. Administration of **ephedrine** systemically brought about cessation of vomiting after 1 day and a reduction of the intraocular tension in 5 days from 50 mm. Hg. to 25 to 30 mm. Hg. The tension remained low without local treatment.

**OPTICOCILIARY RESECTION.**—M. Awerbach (Sovet. vestnik. oftal. 4. 106, 1934) has performed opticociliary resection instead of enucleation in 330 painful blind eyes. These eyes were neither dangerous to the fellow eye nor to life. Pain was relieved and the appearance of the eye remained unaltered.

**SCLERAL ECTASIA.**—A rare case of symmetrical scleral ectasia due to the shape of the orbit is reported by C. Ivanov (*Ibid.* 4: 228, 1934). It occurred in a woman 25 years of age, whose vision had been failing for 5 years. She required a —18 00 D. lens. Horizontally, the eyeballs measured 35 mm. Examination with x-rays revealed the presence of a vertical stenosis of the orbit due to large antra. Exophthalmos had appeared when she was 15 years of age.

**EYELID.—BLEPHARITIS, ULCERATIVE.—Treatment.**—Good results were obtained by T. Krilov and B. Postovtzev (Sovet. vestnik. oftal. 4: 501, 1934) by treating ulcerative blepharitis with **brilliant green** applied to the eyelids 2 to 3 times daily. A 1 per cent. alcoholic solution is more effective than an aqueous solution. Brilliant green and **malachite green** are equally effective.

Good results in the treatment of ulcerative blepharitis by the use of **autogenous vaccines** have been obtained by K. V. Snegirev (*Ibid.* 4: 208, 1934). Every 5 or 6 days he injects 0.2 to 0.5 c.c. of an autogenous vaccine made from the pus obtained from the patient's eyelids. He reports that 32 per cent. of 210 eyes with blepharitis which had not yielded to all previous forms of therapy were cured by this treatment.

**BLEPHAROSPASM, AMBLYOPIA AND HYSTERIA.**—Lazarescu and E. Triandaf (Ann. d'ocul. 171. 175, 1934) observed ocular manifestations in a patient, 18 years of age, who had menstrual disturbances, melancholia and suicidal tendencies. The ocular complications were marked blepharospasm of the right eyelid, anesthesia of the eyelid and of the region around the orbit, and amaurosis of the right eye. Because the patient could fuse with the stereoscope, **hypnotism** and **high frequency current** were employed and complete cure was effected.

**EDEMA.—Etiology.**—Edema of the eyelids may result from sensitization to bacterial protein, according to H. Scarlett (Am. J. Ophth. 17. 242 (Mar.) 1934), who reports 2 cases in which recurrent swelling of the upper eyelids and of the conjunctiva disappeared when dental infection was removed. Cultures taken from the extracted roots showed the presence of hemolytic streptococci.

**NODULES.**—Nodules which had the appearance of tubercles of the episclera and the eyelids in both eyes of a patient, 56 years of age, are reported by W. H. Wilmer (*Ibid.* 17. 99 (Feb.) 1934). She gave a positive tuberculin reaction to 1/100 mgm. of old tuberculin. The diagnosis of tuberculosis was confirmed by the histologic structure of the nodules. Rapid relief from general and local symptoms resulted from treatment with **tuberculin**.

In discussing *differential diagnosis* he points out that tuberculous nodules must be differentiated clinically from episcleritis, nodular scleritis, beginning gelatinous (brawny) scleritis, lymphoma and Boeck's sarcoid of the conjunctiva and eyelids.

In *episcleritis* and in *nodular scleritis* the course of the disease is characterized by improvements followed by relapses. The swellings may be reduced in size by the instillation of adrenalin.

In *gelatinous or brachy scleritis* there is a diffuse inflammation and swelling of the sclera which pits on pressure.

In *lymphomas* the eyeball or the eyelids may be involved. Lymphomas usually appear as prominent, smooth transparent edematous masses which are not nodular. The conjunctival vessels are usually very much enlarged.

In *Boeck's sarcoid* the conjunctiva is not usually involved. When it is affected, the tarsus is usually invaded. Sarcoid of the skin itself, changes in the lymphatic glands, the mucous membrane of the throat and tonsils, and cystic changes in the small tubular bones may be present. In sarcoid of the conjunctiva many minute bodies which have the appearance of follicles may be seen. These vary in size from that of a pinpoint to a chalazion.

Wilmer advocates the following treatment for tubercle-like bodies of the episclera and of the eyelids: **Attention to general health and hygiene** and the use of **tuberculin**. In some cases **surgery** and **radiotherapy** may be indicated.

**PTOSIS.**—A case of recurrent ptosis accompanied by pain, vomiting and elevation of temperature is reported by E. Wolff (*Ann d'ocul* 171: 450 (June) 1934). Ptosis of one eye had recurred 4 times and had disappeared without treatment. A cavernous lymphangioma was demonstrated situated near the border of the orbit. The ptosis was attributed to inflammation or to an intracystic hemorrhage. Wolff associates this syndrome with cavernous lymphangioma. Juler states that in the absence of a tumor this syndrome is suggestive of ethmoiditis.

**ILLUMINATION.—VISUAL EFFICIENCY.**—The relationship between visual efficiency and intensity of illumination is discussed by W. Melanowski (*Klin. Oczna* 12: 80, 1934). He finds that while standard central vision may be obtained with illumination of 50 candle-power, for normal fields of vision and differentiation of color a 200 candle-power light is required.

**IRIDODIALYSIS.—Surgical Treatment.**—B. W. Key (*Am. J. Ophth.* 17: 301 (Apr.) 1934) describes the following method of surgical treatment of iridodialysis.

With a keratome make a fairly broad incision deep in the iris angle directly at the site of the iridodialysis and try to secure a small bit of sclera with a large conjunctival flap as for the modified Lagrange operation. With a pair of scissors enlarge the incision in the conjunctiva, draw the flap of conjunctiva forward with forceps and grasp and withdraw the torn margin of the iris with forceps. Insert a fine silk suture (000 French silk) at the torn margin of the iris, then release the iris, so that it goes back into the anterior chamber. Then bring the double-armed suture through the scleroconjunctival flap at the limbus and tie the suture. The traction of this suture unfolds the iris section and brings it into the desired position by a very slight incarceration of a few fibers of the iris. For support, place 2 sutures under a small amount of tension in the conjunctival flap. Instil **pilocarpine** and apply a dressing to both eyes.

Key cautions against operation (1) in the acute stage, except immediately after injury, (2) on defects which are larger than one-half of the basal attachment of the iris. Operation is indicated in quiet chronic cases in which the dialysis

is large, but not in excess of one-half the base of the iris and in cases in which the dialysis is a definite clinical entity. Associated pathologic changes in the order of frequency are traumatic cataract, hernia of the vitreous, secondary membrane or hypertension.

**IRIS.—INJURIES.**—In a discussion of rupture of the sphincter of the iris produced by a blunt instrument, H. S. Gradle (*Arch. Ophth* 11:92 (Jan.) 1934) directs attention to 3 main types, in order of severity of the trauma: (1) those which involve the anterior superficial stroma with slight involvement of the sphincter muscle; (2) those which involve the sphincter and the posterior pigment epithelium with slight involvement of the anterior stroma; (3) those which involve the anterior stroma, the sphincter, and the pigment epithelium. The second type can best be demonstrated by transillumination. The third type often presents multiple ruptures. In any one of these types irregularity or immobility of the pupil and temporary or permanent weakness of accommodation may ensue.

**IRITIS.—Adrenalin Injections.**—T. Gunderson (*Am. J. Ophth* 17:807 (Sept.) 1934) calls attention to the black deposits which remain at the site of subconjunctival injections of adrenalin employed to dilate the pupil in iritis. This deposit consists of complex organic salts formed from the reduction of ferric chloride resulting from the interaction of the iron in hypodermic needles with the adrenalin hydrochloride. To avoid the black deposits of iris, he advocates the use of a platinum needle or the application of cotton pledgets soaked in adrenalin. Platinum needles are insoluble and free from rust.

**Blood Culture Studies.**—E. F. Traut (*Ibid.* 17:106 (Feb.) 1934) found pleomorphic streptococci in the blood of 5 patients with acute iritis; they were also found in the blood of patients with chronic iritis. These organisms resembled morphologically and culturally those isolated from patients with chronic arthritis. In his technic 20 to 30 c.c. of blood are withdrawn and allowed to coagulate. Some of the serum is centrifuged and then planted in brain or liver broth, dextrose broth and upon chocolate agar plates. Parts of the clot are placed in brain broth and in glucose broth.

**Treatment.**—J. Majoros (*Ztschr. f. Augenh.* 83:16 (Mar.) 1934) reports the results he obtained by the intravenous injection of **sodium salicylate** in 18 cases of iritis and cyclitis. He gave 1 to 2 Gm. (15 to 30 grams) of sodium salicylate in a 10 per cent solution intravenously 3 times daily for only 1 week. The injection was usually followed by a rise in temperature, pain was allayed and disappeared several minutes after the injection, the pupil dilated more readily and the aqueous became clearer. This treatment also controls pain in glaucoma.

**LENS.—CATARACT.—Etiology.**—Slit lamp microscopy of the eyes of 10 furnace men in rolling mills, during and immediately after work revealed that the corneas, anterior chambers and irides were unaffected, and that there were no indications of pathologic heating of the eyes. W. F. Schnyder (*Arch. f. Ophth.* 131:599, 1934) therefore believes that heat-cataract is not due to warming of the lens through heating of the iris.

**Treatment.**—EXTRACTION.—The combined method of cataract extraction shows, according to W. R. Parker (Arch. Ophth 11:183 (Jan) 1934), a lower percentage of complications and a higher percentage of good visual results. His findings are based on comparative results he obtained in 150 cases of extraction of senile cataracts by the combined, simple, and Knapp-Torok intracapsular methods

Attention is directed by D. T. Atkinson (Am J Ophth 17:522 (June) 1934) to the frequency of after-cataract following extracapsular cataract extraction. To avoid this complication he recommends a **posterior capsulotomy immediately following extraction of the lens**. He believes that this method is safer and more effective than intracapsular extraction. After-cataract is usually due to (1) Wrinkling and overlapping of the surfaces of the posterior capsule; (2) thickening of the posterior capsule of the lens (due to regeneration of lenticular cells); (3) cortical lens matter on the anterior surface of the posterior capsule; (4) dense exudates resulting from postoperative iritis or iridocyclitis.

After the lens has been extracted the speculum is removed, the upper eyelid is elevated with the thumb, and a quick stab is made in the center of the posterior capsule with a large von Graefe cataract knife. The eyelid is then allowed to return to its normal position. Moderate preoperative dilatation of the pupil is advisable.

R. O'Connor (*Ibid* 17:809 (Sept) 1934) strongly recommends his method of cataract extraction by the undetached conjunctival bridge. He advises the following procedure:

(a) *Preliminary Incision*—With a 3 mm keratome make an incision just in clear cornea. This incision is made in order to avoid interference with the incision for cataract extraction. With a fine iris forceps draw the pupillary margin of the iris out of the incision and cut it by an upward snip. To avoid dilatation of pupil, use **butyn** as a local anesthetic. (b) *Akinesis*—Retrobulbar anesthesia is unnecessary. (c) Place 2 sutures in the skin of the upper eyelid so that they lie in the middle of each half of the upper eyelid, just above the eyelash line. During the operation these sutures provide the necessary lift and after the operation they furnish a means of closing the eye, holding the eyelids in apposition, by being fastened to the cheek with adhesive plaster. (d) Place a traction suture below the cornea to prevent downward rotation. (e) Do not use a speculum. For the right eye he recommends the use of a Green elevator and for the left eye an ordinary Des Marre retractor because he stands at the patient's right side and uses the right hand, when he operates on the left eye. (f) *Incision*—Make a corneal section starting at about the middle of the cornea and finishing by making a conjunctival bridge about 4 mm wide and about 6 mm long. It is occasionally necessary to make the bridge with forceps and scissors. In deep-set eyes and those with narrow fissures it may be necessary to make the bridge before the corneal incision. To facilitate expression of the lens he uses a tortoise shell spatula which is so flexible that the amount of pressure can be seen as well as felt. Pressure is made over the lower part of the cornea just to start a bend in the spatula. This causes the upper edge of the lens to stretch the bridge and to show on each side. A Fisher needle is inserted into the lens on one side of the bridge and used to lift the lens out from under the other side. By exerting only enough pressure with the spatula to keep the lens from falling back, the lens is not expressed but extracted. When the lens fails to present, he uses the Kalt forceps to obtain a larger bite of anterior capsule. (g) Irrigate to remove cortical matter. (h) Replace the iris pillars. Close both eyes. With adhesive plaster, fasten the sutures which are in the upper eyelid to

the cheek. (i) *Dressing*.—Apply a bland ointment over the eyelashes and eyelid margins, cover with a single thickness of gauze and a cotton dressing. (j) Dressings are changed on the fourth day and the unoperated eye is left open. Both eyes are exposed on the seventh day. The patient walks about from the fourth day and goes home on the eighth.

O'Connor's results were excellent:  $\frac{20}{20}$  vision or better in 84.6 per cent.;  $\frac{20}{30}$  or better in 10.3 per cent, as compared respectively with Knapp's 66.8 and 33.2 per cent.

The operative treatment of cataracts is discussed by A. B. Bruner (*Ibid.* 17.699 (Aug.) 1934). He is opposed to operation for *congenital cataracts* at 10 months of age and prefers to wait until the child is 18 months old. He advocates **needling** of the anterior capsule and, if considerable soft cortex is present, stirring up of the contents with the needle at the time of the discission. In those cases in which there is a poorly developed lens with an opaque capsule and practically no soft cortex, he advises **complete discission** through both anterior and posterior capsules of the lens.

For *juvenile cataracts* usually produced by trauma, the operation of choice is **needling** without preliminary iridectomy.

*Membranous cataract* may be congenital or the result of incomplete absorption of a traumatic cataract or of the persistence of soft cortex after extraction of a senile cataract. Two operations are often necessary for membranous cataracts, i.e., (1) **discission**, to divide the capsular bands in the periphery of the pupil; (2) a **keratome incision** in the cornea through which the membrane is grasped with a small hook and drawn out and cut off.

For *after-cataract* he advises **discission** performed as follows.

The pupil is fully dilated and the eyeball is fixed; a small knife needle, held parallel to the plane of the iris, is introduced in one of the upper quadrants, 2 or 3 mm behind the limbus. The point of the needle first passes through and under the conjunctiva, then through sclerocorneal tissue. The needle is pushed downward until its point comes in contact with the membrane at the lower pupillary margin. The membrane is perforated with a quick thrust and the capsule is divided from below upward with a gentle sawing movement.

To avoid postoperative increased intraocular tension he uses **cocaine** and **epinephrine** instead of atropine. For cataracts in congenitally subluxated lenses he recommends removal of the lens with a **wire loupe**. Bruner (*Ibid.*) advises **preliminary iridectomy** for those cases in which the eye is small, very deeply set in the orbit and the anterior chamber is shallow, when the cataract is hypermature; when there is an associated megalocornea, preexisting chronic simple glaucoma, or when the patient has only 1 eye.

After **linear extraction** he prefers not to use atropine in the first 24 hours after operation.

For *senile cataract*, **extraction by the Kalt or Verhoeff forceps** is an ideal operation. In this method the anterior capsule is grasped below its mid-point. Gentle traction is made downward and then from side to side. As the zonular fibers are torn, the lens comes forward into the pupillary area. Delivery of the lens is performed by gentle pressure applied externally from below. This method is contraindicated when the vitreous is fluid, the capsule is thin, the zonule is weak or the patient has only one eye.

For *anesthesia* he uses (1) either 1 per cent. **holocaine** or 1 per cent. **pantocaine** instilled every 2 minutes for 8 doses, followed by the instillation of 3 drops of 4 per cent **cocaine** and **adrenalin** 1:1000

(2) One per cent **novocaine**, to infiltrate the facial nerve where it crosses the condyle of the upper jaw, and a small infiltration into the skin at the center of the upper eyelid just above the eyelid margin. For intracapsular extraction a moderate amount of dilatation produced by **cocaine** is desirable.

Bruner (*Ibid*) recommends the following procedure:

Place 1 suture in the upper eyelid at the site of the previous injection and a second suture in the tendon of the superior rectus. Insert a Clark eyelid speculum. Fix the eyeball with a nonlocking Elnschnig forceps at a point at the limbus about 5 mm mesial to the lower end of the vertical meridian.

Introduce the cataract knife just behind the limbus. Do not hold the knife horizontally, but direct the point of the knife straight at the fixation forceps until its point has entered the anterior chamber. With the blade of the knife lying in the plane of the iris, pass it across the anterior chamber and bring it into the usual horizontal position. Then make the counter puncture and complete the incision rapidly and smoothly. The incision should follow the limbus and slide under the conjunctiva to produce a conjunctival flap as it comes to the end of the incision. The fixation forceps is removed and iridectomy is performed. The Clark speculum is removed and an eyelid elevator is inserted under the upper eyelid. The eyelid elevator and the superior rectus suture are held by the assistant in one hand, while the lower eyelid is retracted by his other hand. At about "10 and 12 o'clock" in the conjunctival flap, 2 sutures are inserted through the flap and the conjunctiva. The capsule is grasped with capsule forceps in the right hand. It is either torn loose or held on to, as desired. With the hook held in the left hand, gentle pressure is made backward and upward toward the nodal point of the eye until the lens is expressed. Cortical remains are washed out with normal saline solution and the 2 sutures tied and cut off. The pillars of the iris are replaced.

One drop of 1 per cent **atropine solution** is instilled and 1/3000 **bichloride ointment** introduced into the conjunctival sac. The eyelids are held closed by means of the suture previously placed in the upper eyelid. The thread is attached to the skin below by 2 small strips of adhesive plaster. The eye is bandaged and a mask placed over both eyes. A small hole is cut in the mask over the unaffected eye.

*Complications*—Complications in cataract extraction are discussed by O. B. Nugent (*Am J Ophth* 17:135 (Feb.) 1934). In his preliminary examination he considers intraocular tension, blood-pressure, Wassermann reaction, blood sugar, blood urea, basal metabolism, x-ray of the sinus and teeth, smear and culture of the conjunctival sac and examination of the eye with the slit lamp, examination of the gums, teeth, throat, tonsils and lacrimal sac. He advises operation on cataractous lenses as soon after they are discovered as is practicable, without waiting for the on-coming cataract in the other eye to cause an impairment of vision.

The best measure toward an uncomplicated extraction is a well-placed incision. Proper closure of the wound is of paramount importance for a successful result.

**Epinephrine** (adrenalin chloride 1:1000) instilled into the eye before operation lessens the frequency of hemorrhage from the wound at operation. He considers a burst capsule a more dreaded complication than the loss of vitreous.



A **complete iridectomy** is advisable in those cases in which a slit lamp examination has determined the presence of a weak or tense capsule and in those cases in which the pupil fails to dilate. A torn lens capsule should be removed from the eye before the operation is completed.

*Accidental iridectomy* with the cataract knife while making the corneal section cannot always be avoided and it is not very detrimental. Striation of the cornea usually clears up in a few days. *Postoperative hemorrhage* into the anterior chamber is usually caused by a complete or partial separation of the wound. Treatment consists of **rest, atropine** and the application of the **infrared ray**. **Proper suturing of the wound** after extraction will reduce the frequency of this complication.

*Choroidal hemorrhage* during and after cataract extraction occurred in 0.75 per cent of cases. The average intraocular tension in these cases was +3 (Bailliant) and the blood-pressure practically normal. All cases of increased intraocular tension are cases of potential choroidal hemorrhages.

*Glaucoma* after cataract extraction may be due to an iris which is adherent to the wound or to the vitreous body; to remaining portions of lens capsule or cortical substance after extraction; or to frequent attacks of iritis. Treatment consists of **trephining or iridectomy, removal of focal or general infections**, and instillations of **eserine or pilocarpine**.

B. Chance (Am. J. Ophth. 17:929 (Oct.) 1934) reports 3 cases of *massive cystoids* which developed after cataract extractions. The cystoid cicatrices were produced by the accumulation of aqueous, due to the fact that communication between the anterior and posterior chambers was prevented by the iris membrane. He obtained good results by conservative treatment. Instead of excising or puncturing the bladder-like ectasis, he performs **iridocapsulotomy** with a Ziegler knife needle to establish communication between the anterior and posterior chambers of the eye. As a result of this operation, the cyst collapses and shrinking takes place.

**SENILE CATARACTS.—Treatment.**—In comparing the end-results obtained in the **intracapsular and extracapsular operations** for the removal of senile cataracts, D. K. Pischel (*Ibid.* 17:326 (Apr.) 1934) points out that in order to prevent the development of a secondary membrane it is important to remove a large piece of the anterior lens capsule when performing an extracapsular extraction. He concludes that although results in successful intracapsular operation are practically as good as those in extracapsular operation, there were more poor results in his series of cases of intracapsular operations than in an unselected series of extracapsular operations.

**DISCUSSION.—Hypertension.**—R. F. Pereira (Arch. de oftal. de Buenos Aires 9:115, 1934) reports a case of postoperative ocular hypertension which followed a prolapse of the vitreous after discission of an after-cataract. The prolapse was irreducible. After atropine and cyclodialysis had failed, relief was obtained by **transfixion of the iris**. He concludes that (1) the vitreous is impermeable to aqueous; (2) an iridectomy is indicated in all extractions where the cystotome alone is used. In these cases there is a greater possibility of after-cataract necessitating discission.

**DISLOCATED.—Removal.**—An ultraviolet lamp has been designed by H. R. Hildreth (*Am. J. Ophth.* 17:414 (May) 1934) as an aid to the removal of dislocated lenses. Under ultraviolet light the dislocated lens can be seen to glow brilliantly wherever it lies within the eye. He uses carbon arc because of its intensity of radiation. By using a violet glass the greatest part of the visible light is removed but the ultraviolet rays are left.

**LENSES, CONTACT.**—A new contact glass for the correction of all cases of *ametropia* is described by V. Gualdi (*Klin. Monatsbl. f. Augenh.* 92:775 (June) 1934). This contact glass has a single inside curve so that only a series of 6 of these glasses with a scleral curve of 10.5, 11, 11.5, 12, 12.5 or 13 mm radius is necessary to discover which is most comfortably worn. The patient's best vision is determined with an ordinary trial case and the radius of the scleral curve and the correction which should be ground on the anterior surface of the contact lens are noted. The contact glass may then be ordered from the factory.

**LIMBUS.—FISTULA.**—C. T. Eber (*Am. J. Ophth.* 17:921 (Oct.) 1934) reports a case in which a subconjunctival bleb, near the limbus, proved at operation to be a small opening from which exuded aqueous humor. The patient had had rheumatic arthritis since childhood. The cause of the fistula was not determined. The condition is usually accompanied by rheumatic polyarthritis and may be classified with scleromalacia perforans.

**MUSCLES.—IMBALANCE.—Symptoms.**—It is pointed out by F. W. Marlow (*New England J. Med.* 210:309 (Feb. 8) 1934) that headache and asthenopia may be due to errors of refraction, imbalance of the extraocular muscles and impaired general health. In 100 cases in which symptoms were not relieved by correction of the error of refraction, of the manifest muscle imbalance, and of the general conditions, the latent muscle imbalance was disclosed by prolonging the cover test for a week or longer. Muscle imbalances which had been overlooked by the usual methods were demonstrated after prolonged occlusion and relief from symptoms was obtained when the imbalances were corrected.

**MARCUS GUNN SYNDROME.**—G. C. Wilson (*U. S. Nav. M. Bull.* 32:200 (Apr.) 1934) reports a case which presented the Marcus Gunn syndrome. Most cases show unilateral ptosis, strabismus and jaw winking. It is due to an abnormal relationship between the nerve supply of the levator palpebrae superioris and the motor portion of the trigeminus. This case occurred in a boy of 9 years in whom the condition had been present since birth. He had a complete ptosis of the left eye except when his mouth was open, particularly while eating, and opening of the eye was associated with opening of the mouth. His left superior rectus muscle was weak.

**OCCCLUSION.**—W. L. Hughes (*Arch. Ophth.* 11:229 (Feb.) 1934) reports his findings in 10 cases of prolonged occlusion of an eye. Three showed Bell's phenomenon, *i. e.*, the tendency of the covered eye to turn up. To prevent this phenomenon the cover is alternated from one eye to the other.

**OPHTHALMOPLEGIA.**—A case of external bilateral congenital ophthalmoplegia is reported by G. Caocci (Riv. oto-neuro-oftal. 11:162 (Mar.-Apr.) 1934), occurring in a man 35 years of age who since infancy had had a slight drooping of both upper eyelids and limited excursions of the eyeballs. Caocci attributed the condition to an aplasia and hypoplasia of the fourth and sixth nerves and of the cells of the oculomotor nerve without involvement of the nuclei of Perlia and Edinger-Westphal.

**PARALYSIS.—Divergence.**—W. H. Stokes (Arch. Ophth. 11:651 (Apr.) 1934) reports 5 cases of paralysis of divergence. In 2 cases, sisters 68 and 71 years of age, diplopia had existed 2 months and 3 years, respectively. The diplopia was relieved by prisms incorporated in the distance correction. A man 63 years of age had worn prisms for 25 years for relief of diplopia. In a patient 7 years old paralysis of divergence occurred during encephalitis and disappeared in 3 months. In another case paralysis of divergence was complicated by convergence excess. **Resection or advancement of the lateral recti** is indicated in this type of case

**STRABISMUS.—Etiology.**—According to E. L. Armstrong (Am. J. Ophth. 17:291 (Apr.) 1934), the angle of convergence as fixed by the optic axis at the chiasm is the prime factor in the production of strabismus. No strabismus develops when this angle falls within the range of 66 to 70 degrees. *Convergent strabismus* is induced when this angle is narrower and divergent strabismus when it is wider. His conclusions are based on a study of 66 fetuses. He found that all the measurements of the eyes except the angle of the optic nerve change in a constant and regular manner. The angle of the optic nerve curves rapidly and straightens out during the last 2 months prenatally. In cases of wide angles, myopia develops from the increased intraocular pressure caused by convergence

**Classification.**—An etiologic classification has been made by M. A. Pugh (Brit. J. Ophth. 18:446 (Aug.) 1934) of 500 cases of *concomitant strabismus* as follows: 62 per cent showed an error in refraction; 21 per cent showed a psychologic squint, 2 per cent had a squint due to physical defect, *i. e.*, those in which the squinting eye was irrevocably amblyopic. Of the 103 cases of psychologic squints, she found the patients were often emmetropic, 7 per cent were imitative squints, 10 per cent. were jealousy squints, 26 per cent, fear or shock squints; 28 per cent, difficult children (left-handed and self-willed types), and 29 per cent had psychoneurotic parents

**Operation.**—J. W. White (Arch. Ophth. 12:699 (Nov.) 1934) discusses when and how operation should be done for *convergent strabismus* and points out that the following should be considered: (1) The amount of hyperopia and the effect of its correction, by refraction, on the amount of the deviation. (2) The amount of deviation for distant and near vision and in the 6 cardinal fields of vision. (3) The amount and character of the abduction and adduction. This is determined by the screen comitance test. (4) The presence of hypertropia. This is also determined by the screen comitance test. (5) The amount and character of the convergence near point.

Consideration of these points will determine whether an internus muscle should be receded or an externus muscle should be advanced. He points out that it is unreliable to base the surgical procedure on the number of degrees of deviation alone.

A **myocampter** for operating on cases of strabismus with low degrees of deviation has been devised by J. M. Subileau (Ann. d'ocul. 171:507 (June) 1934). The tendon is grasped through the intact conjunctiva and a hook from the myocampter is passed between the muscle and the sclera. The tuck is drawn up to the desired amount, and by bringing the feet of the myocampter together, a toothed clip is clamped into the tuck.

**Orthoptic Training.**—G. P. Guibor (Am. J. Ophth. 17:834 (Sept.) 1934) discusses the possibilities of orthoptic training. He reports his results in 2 series of cases of nonparalytic squint which have been under observation for over 1 year. In series I the refractive error was corrected, occlusion was performed, and the fixing eye was atropinized. In series II orthoptic training was given. The results after 6 months were as follows: In the control group strabismus was corrected in 12.5 per cent. of cases, in the treated series in 50 per cent. After 6 months, 25 per cent. of the cases in the control group showed no squint; in the group which was given orthoptic training, 60 per cent. showed less than 5 degrees of squint with glasses. In 84 per cent. of the cases with 15 degrees of convergence or less there was no squint after training, while in those with a marked deviation only 37.1 per cent. were corrected.

His technic is as follows: One hour of treatment is given each week. Atropine is instilled in the fixing eye. Exercises are given with the stereoscope, using loose hand prisms, bases out, for convergent squint. The strength of these prisms is gradually reduced until fusion is obtained without prisms. By moving the arm of the stereoscope toward and away from the eyes, amplitude of fusion and power of duction are further developed. Prisms, bases in, are then used in increasing strength to develop more power of duction and amplitude of fusion.

The eyes are observed through the front of the stereoscope to detect and prevent alternation; the pointing test is used. By means of this test the card in the stereoscope is described and the fixing eye is determined; the "C" series of Wells charts and split charts are used.

Stereoscopic depth perception is determined by using the Howard apparatus. In his series, 4 patients with alternating squint fused stereoscopically and 3 were unable to do so. Eight patients showed pseudostereoscopic vision early in their orthoptic training and 2 have learned to fuse normally.

In squint cases of more than 15 degrees correction is secured less often but the angle of deviation may be lessened, so that a less radical surgical procedure will be required and patients are familiarized with fusion training.

It is pointed out by J. I. Pascale (*Ibid.* 17:801 (Sept.) 1934) that visual and **orthoptic exercises** improve the vision of the squinting eye and correct the deformity in *concomitant strabismus*. Exercises often have to be supplemented by operation. He begins with exercises for developing rapid, steady fixation of the squinting eye; then he attempts to develop dynamic form vision.

Exercises for form vision are dependent upon an appreciation of the ocular movements and the innervations involved in seeking an object. Coordination of hand and eye by drawing the object or by handling it tend to develop proper projection and orientation. Orthoptic exercises reawaken biperipheral and bimacular vision. For these exercises a set of prisms, a stereoscope and an amblyoscope are necessary.

**THIRD-NERVE PARALYSIS.**—*Operation.*—In children under 15 years of age L. C. Peter (*Ibid.* 17:297 (Apr.) 1934) makes use of the superior oblique muscle as an internal rotator in paralysis of the third nerve. He divides the operation into 3 procedures. (1) A recession of the lateral rectus; (2) tucking of the medial rectus; and (3) transplantation of the superior oblique muscle to the attachment of the medial rectus. The superior oblique muscle is transplanted as follows:

He makes a small incision in the upper eyelid over the trochlea and bluntly dissects the reflected part of the tendon. He grasps it with a tenaculum forceps and severs the tendon beyond the tenaculum proximally to the eyeball. He now exposes the trochlea and opens it without injury to the round tendon. A stout suture is passed through the tendon for control. In a suitable position over the internal rectus he makes a small opening in the capsule of Tenon, from within out and through this opening passes a small hemostat with which he grasps the suture previously inserted in the tendon, draws the superior oblique muscle into place and sutures it to the attachment of the tendon of the medial rectus muscle. The excess length of the superior oblique muscle is cut off. The capsule and conjunctiva are closed and the wound in the eyelid is closed.

**NIGHT BLINDNESS.**—*Etiology.*—D. L. Wilbur and G. B. Eusterman (J. A. M. A. 102:364 (Feb. 3) 1934) report a case of nutritional night blindness which followed a postoperative gastrointestinal complication in which vitamin A deficiency was prominent. The deficiency may arise from gastrointestinal or other disturbances which interfere with normal digestion and assimilation or with metabolic activity.

**OPERATIONS ON EYE.**—In a discussion of the principles of modern surgery in ophthalmology, J. M. Wheeler (Am. J. Ophth. 17:683 (Aug.) 1934) directs attention to the recent and unusual operations for well-known pathologic conditions. He points out that in *retinitis pigmentosa* Mayou (Tr. Ophth. Soc. U. Kingdom, London, 35:357, 1914-1915) reported striking improvement in the visual fields from **corneoscleral trephining**. Mayou assumed that vision was benefited by the improvement in retinal circulation brought about by lowering of the intraocular tension. In 1932, N. D. Royle reported 14 cases of retinitis pigmentosa with improvement in 4 cases as a result of **sympathectomy**. He suggested removal of the first thoracic ganglion after section of the branches.

Under **iridodialysis**, he refers to Jameson, who advocates suturing the iris near an incision in the limbus of the cornea. Wheeler recommends the following simple surgical procedure for iridodialysis: a keratome incision is made through the limbus at the site of the opening in the iris, an attachment is secured by carrying a tiny shred of tissue from the torn edge of the iris into the wound of the limbus.

In *glaucoma cyclodialysis* with **iridectomy** is done as follows: The scleral incision is made about 12 mm. from the limbus between the recti muscles; the choroid, ciliary body and iris are separated from the sclera and cornea through a 3 mm scleral incision. The keratome enters under cover of the dissected conjunctival flap and an iridectomy is made without making a second conjunctival incision. This operation produces a permanent anterior chamber and furnishes permanent drainage through the original drainage system.

In *pulsating exophthalmos*, caused by communication between the internal carotid artery and the cavernous sinus, **ligation** or **resection of the internal carotid** or of the **common carotid artery** in the neck is the proper surgical procedure.

For *exophthalmos due to Graves' disease*, Wheeler recommends a combined operation: (1) Shortening of the fissure by preparing a groove in the outer part of one eyelid and a tongue of denuded tissue in the corresponding part of the other eyelid. The epithelium is then removed from the contact areas of both eyelids and the eyelids are sutured to each other to produce the desired amount of shortening (2) Reattachment of the external canthal ligament behind the orbital margin. In this way the eyelid margins are put on stretch and the fissure is narrowed.

In more pronounced cases he recommends his combined operation (described above) plus Goldstein's "recession of the levator palpebrae superioris" in which the levator is dissected free from the conjunctiva and orbicularis and is receded so that its action is reduced. He points out that in progressive exophthalmos following thyroidectomy Naffziger decompresses the orbit by removing its roof through an intracranial approach and later Naffziger and Jones removed not only the roof of the orbit, but the roof of the optic canal and slit the ligament of Zinn. For pulsating exophthalmos due to a meningocele in the orbit, W. E. Dandy (Arch. Ophth. 2: 123 (Aug.) 1929) took a graft from the outer table of the skull and made a roof for the orbit to replace a congenital defect. The result was excellent.

In discussing **grafts of the cornea** he states that homoplastic grafts take readily, but opacification of the graft usually follows. Castroviejo believes that a rectangular graft is better than a circular one and he finds that the graft of the donor and the opening in the cornea of the recipient should be correspondingly beveled, so that the anterior surface of the graft is larger than its posterior surface, corneal sutures are not necessary and a thin conjunctival flap over the graft is the best means for holding the graft in position. The conjunctiva protects the graft and enhances its nutrition.

In *detachment of the retina* the object is to secure a reaction in the choroid so that the inflammatory process will cause adhesions between the choroid and the retina. Wheeler is of the opinion that reattachment should be effected with less traumatism. In his experiments, he found that he could make a definite line of edema in the choroid merely by drawing a needle charged with a **high-frequency current** along the surface of the sclera. A circle may be drawn on the sclera to enclose a retinal hole. A good inflammatory reaction in the choroid may also be obtained by the **Shahan thermophore**.

**IRIDOCYCLITIS.**—For cases of chronic iridocyclitis with increased tension, A. Fuchs (Arch. Ophth. 11:591 (Apr.) 1934) advises: (1) **Iridectomy**, in those cases in which the posterior adhesion has not become complete. (2) **Transfixion** or **partial transfixion with immediate iridectomy** when seclusion of the pupil and iris bombé are present. (2) **Repeated punctures** of the anterior chamber for serous iritis and for iritis in diabetics after cataract extraction. (4) **Optical iridectomy** performed above to improve vision if the pupil is small. This produces a sufficiently large opening and provides a coloboma if extraction becomes necessary. (5) **Preliminary iridectomy** and **extracapsular extraction** are advised for complicated cataracts. (6) For **discission** an operation with 2 needles is advised.

**OPHTHALMOLOGY IN OBSTETRICS.**—M. B. Bergmann (Am. J. Ophth. 17:141 (Feb.) 1934) discusses the relationships between ophthalmology and obstetrics. The most common and important ocular findings in pregnancy are albuminuric retinitis, optic neuritis, neuroretinitis, retinal and papillary edema or choked disc, retrobulbar neuritis and amaurosis. These findings often serve as guides in the diagnosis and management of the toxemias of pregnancy. An edematous halo surrounding the disc usually indicates a general toxicosis and may be of inestimable value with regard to the expectant treatment.

**OPTIC NERVE.—ATROPHY, HEREDITARY** (*Leber's Disease*).—A. J. Bedell (*Ibid* 17:195 (Mar.) 1934) reports 8 cases of hereditary atrophy of the optic nerve which occurred in 5 generations, involving 3 parent stocks. Transmission takes place through the maternal side. The atrophy in these cases was traced to one woman in whose descendants it recurred repeatedly. The other two stocks were free until contaminated by her stock. Hereditary optic atrophy, Leber's disease, is characterized by rapid loss of vision, which usually begins at puberty or in early youth, atrophy of the optic nerve, contraction of the visual field and a central scotoma.

**CYST.**—C. C. Coleman and E. Hill (Arch. Ophth. 11:42 (Jan.) 1934) report a case of cyst of the optic nerves and chiasm associated with an epithelioma of Rathke's pouch in a girl 14 years of age. She had complained of frontal headaches, drowsiness and loss of vision. Examination revealed optic atrophy and a dilated third ventricle which was suspicious of tumor in the region of the optic chiasm. When the cystic optic chiasm and right nerve were incised at operation, 4 or 5 c.c. of yellow fluid escaped. Vision improved but the patient died 4 months later. At autopsy an epitheliomatous tumor of Rathke's pouch was found with cystic dilatation of the preoptic recess. This did not communicate with the remaining cavity of the third ventricle, but invaded the optic chiasm and optic nerves.

**MENINGIOMA.—Diagnosis.**—K. Mylius (Ztschr. f. Augenh. 82:257 (Feb.) 1934) reports a case of a meningioma of the olfactory groove because it is a tumor of especial importance to the oculist. It is characterized by anosmia, degenerative descending optic atrophy with central scotoma on the side of the lesion, contralateral papilledema, and, in advanced cases, other symptoms of involvement of the frontal lobe. In basal glioma general manifestations of brain

tumor, *viz*, headache, vertigo, vomiting, apraxia, static ataxia, and motor aphasia occur earlier than in tumors of the olfactory groove. Because of its rapid growth, gliosarcoma is less likely to cause difficulties in diagnosis.

Meningioma in the tuberculum sellæ may grow along the base of the frontal lobe, but the anosmia develops after other symptoms and after pressure on the chiasm has produced heteronymous hemianopic field defects. The x-rays and lumbar punctures may be of some diagnostic assistance.

**NEURORETINITIS.**—J. D. McCulloch (*Ann. d'ocul* 171:457 (June) 1934) reports a case of bilateral neuroretinitis which appeared as a complication of grippé. It occurred in a patient 45 years of age who presented the following: (1) Vision—there was no light perception; (2) fundi—optic discs were pale and their markings were hazy. The optic discs were surrounded by exudates and by dilated veins. No hemorrhages were found. Complete atrophy developed within 2 weeks. The Wassermann reaction was negative and the teeth, sinuses and urine were normal. Optic atrophy is a rare complication of grippé.

**OPTIC ATROPHY.**—*Treatment.*—It was found by D. Lees (*Ibid* 171:449 (June) 1934) that optic atrophy occurred in only 8 per cent. of a series of cases of neurosyphilis which he treated with **tryparsamide**. He precedes the treatment with tryparsamide (pentavalent arsenic) by administering **iodides** for 15 days, followed by injections of **bismuth** for 1 month. This procedure is adopted in order to avoid the Herxheimer reaction. Intravenous injection of tryparsamide is then given weekly beginning with 0.50 Gm (7½ grains) and gradually increasing the dosage until 2 or 3 Gm (30 to 45 grains) are given. Rest periods are given during the course of treatment. From the ocular rather than from the neurologic point of view tryparsamide improves and “stabilizes” the disease.

**OPTIC NEURITIS, RETROBULBAR.**—A. Magitot and Desvignes (*Ibid* 171:53 (Jan.) 1934) report a case of retrobulbar neuritis with central scotoma in a young woman. Although the central scotoma disappeared in 15 days, angioscotometry revealed an enlargement of the blind spot of Mariotte and a deficiency of the lower vascular shadows with conservation and widening of the upper vascular shadows. The vascular shadows and the blind spot of Mariotte became normal when the patient was cured.

**Etiology.**—W. I. Lillie (*Am. J. Ophth* 17:110 (Feb.) 1934) directs attention to the fact that retrobulbar and optic neuritis are manifestations of some systemic condition. He finds that the nasal accessory sinuses or the teeth are seldom the cause. Speaking generally, the prognosis in cases of retrobulbar neuritis is good; in optic neuritis it is poor. Since retrobulbar or optic neuritis is rarely local, a complete general and neurologic examination is necessary to determine the etiologic factor. He has found that the most common cause of retrobulbar and optic neuritis is *multiple sclerosis*. In multiple sclerosis, the vision improves regardless of the treatment employed.

Multiple sclerosis afflicts about 9 persons in every 100,000. It is usually insidious in onset and occurs most frequently in the second and third decades of life. The most common symptoms are motor or sensory disturbances of the lower extremities and visual disturbances (diplopia and central scotomas).



The spinal fluid usually shows an increase in the number of cells. The colloidal gold curve is of the zone I type, signifying parenchymatous degeneration. The only other disease that produces such a curve is general paresis.

The next most common cause of retrobulbar and optic neuritis is *meningoencephalitis*. In meningoencephalitis optic neuritis is more common than retrobulbar neuritis. It lasts longer, but does not usually recur. A diagnostic sign of meningoencephalitis is the presence of marked increase of cells in the spinal fluid.

*Encephalitis periaxialis diffusa* is a rare disease in which retrobulbar or optic neuritis occurs. *Tumor of the basal portion of the frontal lobe* may produce retrobulbar or optic neuritis associated with adjacent cerebral manifestations.

*Toxic amblyopia*.—Retrobulbar neuritis due to nicotine poison is characterized by a slowly progressive reduction of the central vision, usually in both eyes. The patient sees better in reduced illumination. Pallor of the discs may be present in chronic cases. Relative or absolute central scotomas may be present. Lillie has never seen nicotine poisoning due to the smoking of cigarettes, but to the smoking of cigars or pipes and to the chewing of tobacco.

The treatment of toxic amblyopia consists of (1) **pilocarpine sweats**; (2) **abstinence from smoking cigars, pipes or from chewing tobacco**. *Metabolic and nutritional disturbances* are contributing factors. *Nicotine poisoning* is relatively more frequent in cases of diabetes, anemia or brain tumors. *Ethyl alcohol* produces the same syndrome. Sudden loss of vision is due either to *methyl alcohol* or to some impurity in ethyl alcohol. Loss of vision may be permanent but useful sight is usually recovered. Optic neuritis due to *lactation* is rare. In these cases breast feeding should be discontinued to avoid serious injury to vision.

*Lead poisoning* may produce retrobulbar neuritis. **Calcium lactate** and **parathormone** are used to precipitate the lead. *Thallium poisoning* resulting from the use of Koremlu cream as a depilatory may produce retrobulbar neuritis.

*Paranasal sinusitis* in only 1 case out of 500 was found responsible for retrobulbar or optic neuritis.

A small percentage of cases of retrobulbar neuritis is *congenital* and may be associated with strabismus or be the cause of the strabismus. *Hereditary optic atrophy* (Leber's disease) and *syphilis* are other rare causes.

Lillie points out that the central field may show a small relative central scotoma or there may be a complete amaurosis. The course in retrobulbar neuritis is the progression from a small relative central scotoma to a small absolute central scotoma, cecocentral scotoma, temporal islands of vision and complete amaurosis. This order may be reversed, especially in acute cases.

**Treatment**.—M. Renedo (Arch. de oftal. hispano am 34 177 (Apr) 1934) advocates **suboccipital injection of air** in retrobulbar neuritis. In 1 patient who had optic atrophy of 7 years' duration improvement followed in 1 month after a series of injections. Before injection the patient's vision was fingers at 2 meters in the left eye and fingers at 10 meters in the right eye, with temporal hemiachromatopsia. After 15 to 20 c c of air had been injected the vision improved to 9/10 in the right eye and 1/5 in the left.

N. N. Ray (Brit. J Ophth. 18: 170 (Mar ) 1934) reports a new method of treatment of chronic retrobulbar neuritis and toxic amblyopia caused by heavy metals and acute infectious diseases. He recommends a course of 6 deep intramuscular gluteal injections of **contramine**, an organic sulphur compound, every 48 hours. He also prescribes a mixture of **glycerophosphates** and **strychnine** to be taken internally. Amblyopias caused by tobacco and quinine were not included in this series of 150 cases. The method is contraindicated in chronic alcoholism, chronic retrobulbar neuritis of disseminated sclerosis, in nephritis, diabetes, or syphilis unless there is a negative Wassermann after antisyphilitic treatment.

**PAPILLA —PIGMENTATION.**—It is pointed out by G. Michail (Arch d'opht. 51 129 (Mar ) 1934) that pigmentation of the optic papilla, whether congenital or pathologic, arises from the blood, the choroid, the retina or the glial tissue. He describes 4 cases. In 1, a plaque of pigment was seen on the optic disc in a case of papilledema caused by a tumor of the frontal lobe. In another a linear streak of pigment was seen on the disc 8 months after fracture of the optic canal. In a third patient, stippled pigmentation of part of the pale disc was seen in a case of congenital zonular cataract. The fourth case presented serrated pigmentation of the disc, melanosis of the iris and sclera, pigment on the anterior lens capsule and pigmented cutaneous moles.

**SURGERY OF OPTIC NERVE.**—H. Schloffer (Med Klin 30 421 (Mar 29) 1934) recommends resection of the roof of the optic canal for the relief of pressure on the intracranial portion of the optic nerve. This procedure is indicated in cases of *tower skull* when vision fails and in cases of *pressure of a sclerotic carotid artery* upon the optic nerve. The latter condition may be evidenced by nasal constriction of the visual field and by x-ray suggestion of calcified carotid walls.

**SYNCHYSIS SCINTILLANS.**—J. L. Pavia (Rev oto-neuro-oftal 9 93 (Mar ) 1934) demonstrated by moving pictures and stereoretinography that in synchysis scintillans the filaments start from the fovea and spread out like a fan toward the ora serrata.

**TUBERCULOSIS OF THE OPTIC NERVE**—Five cases are reported by I. Sicharulidze (Sovet vestnik oftal 4 506, 1934) of tuberculous optic neuritis which were treated with **tuberculin**. Good vision was recovered in 4 cases and vision was lost in the fifth case due to optic atrophy.

**TUMORS OF OPTIC NERVE.**—P. DeLong (Am J Ophth 17 797 (Sept ) 1934) discusses primary tumors of the optic nerve and reports 1 case. He states that all primary intraneural tumors of the optic nerve are gliomas which are congenital and depend upon some abnormality of the neuroglia. The earlier the type of cell in the histogenetic series of development, the more malignant is the tumor.

**ORBIT.—TUMORS.**—A case of pure *fibroma* of the orbit in a man 25 years of age is reported by W. H. Stokes and W. F. Bowers (Arch Ophth. 11 279 (Feb ) 1934). Partial ptosis of the left upper eyelid occurred 4 years previously. Proptosis, diplopia and pain had followed. The tumor was found

attached to the periorbita, behind and lateral to the eyeball. It was removed through an incision in the eyebrow. The fibroma was composed of a mature type of cell.

A. Stroopov (Sovet vestnik. oftal. 4:210, 1934) reports an unusual case of *malignant tumor* of the temple and orbit in a girl 17 years of age. Following an injury, a malignant endothelioma of the cranial periosteum had developed. It involved the right temporal and frontal bones and its largest portion was between the two thin layers of bone of the roof of the orbit. Exophthalmos, displacement of the eyeball down and in, and increased intracranial pressure were present. Operation was followed by recurrence, necessitating another operation 4 years later. Six years have now elapsed without recurrence and the patient is well.

Seven cases of tumors of the orbit are reported by G. Hardy and W. F. Hardy (Am. J. Ophth 17 18 (Jan) 1934). One was an *adenocarcinoma of the lacrimal gland*, another a *pseudotumor*, and still another a *perineural fibroblastoma of the optic nerve*. Diagnosis was confirmed histologically.

*Tumors of the orbit* are comparatively rare. The more anteriorly the growth is situated, the better is the prognosis. In primary tumors of the optic nerve the prognosis is unfavorable. In their series of cases the following points were diagnostic of *glioma of the orbit*: unilateral exophthalmos, biopsy with a resultant diagnosis of glioma. The points against the diagnosis of glioma were the preservation of fair vision and the presence of a positive Wassermann reaction.

**XANTHOMATOSIS.**—R. M. Rogers (*Ibid* 17:1141, 1934) reports a case of xanthomatosis in an adult with diabetes insipidus, yellow pigmentation of the skin of the eyelids, and bilateral exophthalmos due to multiple tumors of the orbits. X-ray examination showed enlargement of the sella turcica and changes in the posterior clinoid processes. The cholesterol content of the blood was increased. Biopsy showed lipid deposits in the tissue. The clinical manifestations are due to an infiltration of the reticulo-endothelial cell with lipoids, chiefly cholesterol and its esters, which cannot be properly excreted and act as irritants to body tissue. The etiology of the disease is unknown.

Two additional cases of xanthomatosis of the orbit in which there were no other symptoms of xanthomatosis except hypercholesteremia, are reported by A. Knapp (Arch Ophth 11:141 (Jan) 1934). The tumor was found below the upper bony margin of the orbit. It produced proptosis. X-ray examination showed a defect of the frontal bone not connected with the nasal sinuses. Xanthomatosis is the result of the phagocytic action of the reticulo-endothelial system, which stores an excess amount of lipoids and produces hyperplastic nodular lesions. The growth is cured by operation and does not recur.

The Schuller-Christian syndrome, which resembles it, occurs only in young children and usually involves the ethmoid and the lesser wing of the sphenoid bones.

J. M. Wheeler (*Ibid* 11:214 (Jan.) 1934) reports a case of Schuller-Christian disease (xanthomatosis) in a boy 3 years of age. Autopsy showed generalized xanthomatosis of the bones, dura, hypophysis, infundibulum,

periosteum and orbits, with involvement of the skin and of the thoracic and abdominal organs

**PERIMETRY.—*Tangent Screen.***—C Berens, D. Kern and B F. Payne (Am. J. Ophth. 17:826 (Sept) 1934) describe a tangent screen with certain features which make it practical for clinical and scientific examination. The background, which is neutral-gray, produces less retinal fatigue, so that the after-images are less disturbing. The markings drawn in brown on the neutral gray cloth are almost invisible and thus facilitate charting and the approximate estimation of the size of scotomas. A working distance of 75 cm. is practical for mapping central visual fields, blind spots, scotomas and angioscotomas, diplopia fields, and fields of monocular fixation. Standardized daylight illumination of 7-foot candles increases the accuracy of the results. Spherical test objects add to the accuracy because the visual angle of the test object subtended is not affected by rotation of the test object.

**TONOMETRY.—*Pernicious Anemia.***—In most cases of primary anemia G F. Suker (*Ibid.* 17:125 (Feb) 1934) found that the tension was noticeably reduced and returned to normal limits only when the blood condition was improved, and that in cases of pernicious anemia some patients had a tension which was nearly normal when the blood constituents were far below normal.

He concludes as follows: There is a marked lowering of the intraocular tension in nearly every case of primary anemia and particularly in the agranulocytosis and pernicious anemias. The intraocular tension returns to nearly normal or normal when the blood picture improves. Decreased intraocular tension does not tend to produce intraocular complications or any functional complications. When the hemoglobin and the number of red blood corpuscles and white blood corpuscles decrease the intraocular tension drops and when they increase, tension rises. The fundus has a waxy hue in all cases of anemia.

**VISUAL FIELDS.**—Greater uniformity in methods of field taking is urged by A H. Thomasson (Arch. Ophth. 12:21 (July) 1934). He stresses the importance of recording the visual acuity, the size and color of the test object, and the radius at which it is used; the quality and intensity of the illumination. He advocates the use of standardized charts and daylight illumination. Examination of the central field (within 25 degrees) must be made on a tangent screen. If vision is 20/20, he uses a 0.5 mm. white object at 1, 2, 3, and 4 meters and a 2 mm. red or green object at 2 or 3 meters. If vision is reduced, larger test objects are necessary. For examination of the peripheral field he uses a 5 mm. white object.

***Binasal Contraction.***—In 12 cases of binasal contraction of the field of vision which occurred as a result of intracranial disease reported by C. Vincent and E. Hartmann (Ann. d'ocul. 171:193 (Mar) 1934), 8 of the cases had choked discs and only 2 showed optic atrophy. The relatively large number of cases of choked discs leads the writers to conclude that choked disc or the factors which produce it (cerebrospinal hypertension) plays an important part in the production of binasal hemianopsia. In some cases this defect in the field of vision is due to the local direct effect of the primary tumor or inflammation.

In other cases it is due to remote disturbances. The function of the nerve fibers is disturbed by edema of the optic nerve and optic disc, increased tension of the fluid within the sheaths of the optic nerve, and retardation of the circulation of the eye. They believe that the nerve fibers on the temporal side of the retina are more delicate and are therefore more readily affected than those on the nasal side of the retina. Contraction of the nasal field of vision is also found in glaucoma, optic atrophy and following marked loss of blood.

**Hyperthyroidism and Exophthalmic Goiter.**—P. L. Drouet, P. Jeandelize and A. Gault (*Ibid.* 171:465 (June) 1934) discuss the modifications of the field of vision in the syndromes of hyperthyroidism and of exophthalmic goiter. They stress the importance of bitemporal contraction of the field of vision. This defect may indicate a neuroendocrine syndrome. The pituitary gland is apparently associated with hyperthyroidism, particularly when the bitemporal contraction of the field of vision is associated with the finding of hypophyseal elements in the blood or urine. They conclude that in exophthalmic goiter both hyperthyroidism and hyperpituitarism are present but in the parabasedow syndrome only hyperpituitarism is present. In the parabasedow syndrome, exophthalmos, goiter, tremor, and tachycardia are present but the basal metabolism is normal.

**POSTERIOR CHAMBER.—EPITHELIAL CYST.**—C. W. Tooker (*Am. J. Ophth.* 17:41 (Jan.) 1934) gives the clinical history and microscopic anatomy of an enucleated eye in which an epithelial cyst was found in the posterior chamber. The cyst was traumatic in origin, due to implantation of epithelial cells which had proliferated from the root of the iris or ciliary body. It was seen clinically and transilluminated well. Epithelial cysts of the posterior chamber, originating from the iris, the ciliary body, or from implanted epithelium, are rare.

**RETINA.—DETACHMENT.**—*Etiology.*—A Hagedoorn (*Ibid.* 17:400 (May) 1934) produced a *rupture* of the retina in the eyes of 3 rabbits by suction of the vitreous through a cannula. The cannula was inserted into the vitreous through an opening in the sclera near the limbus. From his experiments he concludes that in a healthy rabbit's eye a rupture of the retina alone is not followed by a detachment of the retina.

**Surgical Treatment.**—For the surgical treatment of detachment of the retina, A. Vogt (*Arch. Ophth.* 12:842 (Dec.) 1934) advocates the use of momentary multiple punctures with the **electrolysis** needle (cathode) in the margin of the hole and in the hole itself. An intensity of only from 0.5 to 1 ma. of current is necessary.

L. C. Peter (*Ibid.* 11:262 (Feb.) 1934) obtained satisfactory results in 8 cases of retinal detachment by Walker's method of **electrocoagulation**. He advocates placing the needles about 2 mm. apart so as to include the entire tear.

In another article (*Am. J. Ophth.* 17:924 (Oct.) 1934) he describes his technic and recommends the micropuncture or electrocoagulation method with the Walker unit and needles. Peter is of the opinion that the electrocoagulation

method produces a higher percentage of good results because it is more accurate and less traumatising than other methods.

The patient is prepared as follows:

Rest in bed for several days before the operation, proper elimination, and restriction of fluid intake. Cultures are taken, the culdesacs of the conjunctiva are cleansed, the patency of the lacrimal drainage system is investigated, the pupil is fully dilated and a sterile dressing is applied. **Morphine** with **atropine** is given hypodermically. For anesthesia, instillations of **cocaine** and retrobulbar injections of 2 per cent **procaine solution** are employed. The conjunctiva over the operative area, and the sheaths of the muscles are infiltrated with procaine solution.

The meridian in which the tear is located is designated by the numeral on the face of a clock. The distances from the macula and from the ora serrata are determined in disc diameters.

To obtain adequate exposure of the entire field of operation the following is recommended. When operating on the temporal side canthotomy may be of assistance, the use of a Guist speculum, free incision of the conjunctiva and capsule, detachment of the recti muscles, and the use of double-armed sutures for the muscles. The entire field of operation should be exposed before the punctures are placed. The sclera is exposed and dried, and an outline is made on the sclera of the exact area to be treated.

The coagulation points are placed 2 mm apart, overlying the detachment. To include invisible peripheral tears near the ora serrata a second line of needles is placed 2 or 3 mm anterior to the line and about 2 or 3 mm posterior to the ora serrata. To insure proper drainage, 2 or 3 large needles are placed midway between these two lines. When the coagulation punctures are completed, the silk threads are grasped and slowly withdrawn.

Peter recommends the following after treatment. Close both eyes with a pressure bandage. Place the patient so that his head is in a favorable position for drainage from the eye. Dress the eyes on the third and fifth days and on the seventh day, examine the fundus and remove the conjunctival sutures. Dress daily for another week. Prescribe pinhole goggles. Remove muscle sutures in 2 weeks. Allow the patient out of bed in 3 weeks.

At the end of 7 days the retina is usually flat. The vitreous gradually clears and the small areas of coagulation become white and circumscribed and surrounded by deposits of pigment. Adhesions usually become firm at the end of 4 weeks and the patient resumes his normal activities in about 6 weeks.

Peter stresses the importance of regarding areas of choroiditis as the probable sources of leakage when frank tears cannot be found. These areas should therefore be included when the area of retinal detachment is coagulated.

Surgical treatment is recommended by P. Veil and Felgines (*Arch. d'opht.* 51: 158 (Mar.) 1934) for retinal detachment in patients whose retinas do not readily reattach after rest in bed and the wearing of stenopæic lenses. They use **galvanocautery** for small, large or multiple tears or disinsertions of the retina. They advocate secondary operation with a fine pointed galvanocautery for those cases in which diathermocoagulation is ineffective.

A. Vogt (*Ztschr. f. Augenh.* 84: 18 (Aug.) 1934) reports a case in which reattachment occurred after 1 closure of a hole in a retinal detachment which had persisted for  $7\frac{3}{4}$  years.

A. Zamenhof (*Klin. Oczna* 12: 38, 1934) describes his own method of surgical treatment of detachment of the retina. After localizing the tear, he blockades it with a semicircle of nonperforating diathermically coagulated areas.

1.5 mm. in diameter placed 2 to 3 mm. from each other. He then perforates each coagulated area with the **electrocautery**.

For the operative treatment of retinal detachment C. B. Walker (Am. J. Ophth. 17:1 (Jan.) 1934) recommends his own **diathermy** unit with threaded, iridium-hardened platinum micropins which have uninsulated stops. He reports 1 case in which it was used successfully and describes his method in detail.

He concludes as follows: Diathermic equipment is necessary in ophthalmic practice; diathermy by micropuncture alone produces the greatest average success with the least labor. However, it is probable that in some cases this method may prove to be more successful when combined with the Gonin or Lindner-Guist operations; with the micropins, overdosing does not occur and the sclera receives a small degree of treatment. Iridium-hardened platinum may be sterilized by heating to redness in a Bunsen flame.

**PRESSURE.**—In every case of increased intracranial pressure J. Sobanski (Klin. Oczna 12:146, 1934) advocates the determination of the venous and arterial retinal pressure. The ratio of these pressures indicates when a trephine operation of the skull is necessary to prevent blindness. He finds that venous retinal pressure is closely related to the intracranial pressure and that the pressure at which a venous pulse appears is approximately equal to the intracranial pressure. In a report of 28 cases of increased intracranial pressure he found that choked disc depends on the ratio between the pressure in the retinal arteries and veins and that choked disc appears when the ratio of the venous to the arterial pressure becomes 1:15.

Seven cases in which intracranial hypertension followed *traumatism* are reported by A. Arnaud and P. Guillot (Ann. d'ocul. 171:735 (Sept.) 1934). In suspected cases the ophthalmotonometer or dynamometer may be used to detect the existence of intracranial hypertension. When correlated with the clinical symptoms, increased intracranial hypertension may indicate the necessity for surgical intervention.

**VITAMIN A DEFICIENCY.**—P. C. Jeans and Z. Zentmire (J. A. M. A. 102:892 (Mar. 24) 1934) describe a clinical method for determining moderate degrees of vitamin A deficiency by the use of the electrically illuminated Birch-Hirschfeld photometer. In 213 children, they determined the sensitivity to light following partial dark adaptation. Forty-five had subnormal dark adaptation and half of these, when given a diet which included **cod-liver oil**, regained normal adaptation in about 12 days.

**SCLERA.—SCLEROMALACIA PERFORANS.**—Four cases of this disease are reported by J. Van der Hoeve (Arch. Ophth. 11:111 (Jan.) 1934). It is characterized by degeneration of the sclera, with the development of holes in any part of the sclera. These holes may or may not be covered by conjunctiva. Cloudiness of the cornea and uveitis may follow. Scleromalacia perforans is found in middle-aged and in old people and may be associated with polyarthritis.

**TUMORS.—GLIOMA.—Treatment.**—A case of bilateral glioma in a year-old child is reported by H. Barkan (*Ibid.* 11:20 (Jan.) 1934) which was treated by **radium**. The right eye was enucleated. In the superior temporal quad-

rant of the left eye was a gray-white mass of 5 disc diameters adjacent to the disc. He inserted 2 five-mg. needles of radium through the sclera at the site of the tumor. He repeated this radium treatment 3 months later. Regression of the tumor took place but retinal detachment and blindness ensued. The eye was enucleated about 1 year later. Histologic examination revealed the presence of fresh tumor masses.

**UVEA.—UVEITIS, CHRONIC.**—A L Brown (*Ibid.* 12.730 (Nov.) 1934) discusses chronic uveitis from the bacteriologic and immunologic standpoints. He concludes as follows: (1) The bactericidal power of the aqueous and vitreous is negligible. (2) The normal intraocular contents do not inhibit the growth of the streptococcus within the eye. Autogenous blood serum or whole blood within the eye definitely inhibits growth. (3) Foci of infection implanted in parts remote from the eye do not produce ocular inflammation. Inflammation of the eye resulted in only 1 of 80 animals in which this experiment was performed. When the eye was sensitized by a toxic filtrate of the organism, the remote foci then activated the eye in 25 of 30 cases. After such sensitization, when the same organisms were injected intravenously the eye was activated in 98 of 100 cases. (4) Streptococci which produced iritis when injected into the carotid artery, affected the eye in only 1 of 25 cases when injected intravenously. (5) Organisms grown within the eye or with uveal tissue *in vitro* became attenuated for the eye after repeated passages. The original strain carried simultaneously was unaffected. (6) The blood cultures of 81 patients who had iritis and uveitis were negative, except in 2 cases. These 2 had gross generalized inflammation. (7) Bacteriologic examination of the aqueous and uveal tissue in chronic uveitis and recurrent iridocyclitis gave negative results.



# OTORHINOLARYNGOLOGY

*by*

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## PHARYNX AND TONSILS.—AGRANULOCYTIC ANGINA.—

According to F. A. Burton (Ann. Otol. Rhin. and Laryng. 43:472 (June) 1934), some progress has been made in the diagnosis and treatment of this disease, with the result that a rapidly fatal mortality, formerly of 80 to 90 per cent, has been reduced to about 26 per cent. This writer asserts, however, as is well known, that a previous attack does not confer immunity, and the so-called recovered cases often become recurrent ones.

**Etiology.**—J. Groen and C. J. Gelderman (Nederl. tijdschr. v. geneesk. 78:3444 (July 28) 1934) sought to determine what drugs had been used by patients who were being treated for agranulocytosis. Of 13 cases observed during the past 3 years, *neoarsphenamine* was a causative factor in 2 instances. Nine patients had been taking some drug containing *antipyrine* or *amidopyrine*, often in combination with some other compound, before the onset of their symptoms. In 1 case recovery of the number of leukocytes and of the necrotic angina was observed after discontinuance of the amidopyrine medication. In 2 cases an inquiry among the physicians who had been treating the patients before their admission revealed only the use of *acetylsalicylic acid*, *sodium salicylate* and *quinine sulphate*; but the possibility that other drugs had been taken could not be excluded. Five additional cases, observed elsewhere, are described. In each case some compound containing amidopyrine had been used. The authors maintain that an outbreak of agranulocytosis may follow the use of various drugs. Among those, antipyrine and amidopyrine have a definite etiologic significance. The possibility of a similar effect from the use of other antipyretics and hypnotics (especially the two barbiturates) must be borne in mind. The danger of an agranulocytotic syndrome occurring after the use of drugs is probably restricted to certain allergic individuals.

Many present conceptions about agranulocytosis must be revised, a toxic etiology of agranulocytosis appears to be the rule rather than the exception. During the administration of antipyrine or amidopyrine, a continuous supervision of the leukocyte count is imperative and this fact is emphasized by A. M. Hoffman, E. M. Butt and N. G. Hickey (J. A. M. A. 102:1213 (Apr. 14) 1934). As a result of their investigation, they believe that the common factor in amidopyrine, dinitrophenol, benzene, arsphenamine, ortho-oxybenzoic acid and hydroquinone, all of which have produced neutropenia experimentally or clinically, is the *benzene ring*. Whether the latter is the actual toxic agent in the production of neutropenia needs further experimentation, part of which is now being undertaken. The work of these investigators points to amidopyrine as having a definite effect on myeloblastic tissue similar in man and in rabbits. Whether this is an individual susceptibility of the nature of an allergic reaction remains to be determined. Until this has been done, certainly the use of amidopyrine, alone or in combination with other drugs, should be restricted, as has been pointed out, to patients having leukocyte counts several times a week.

S. S. Bohn (*Ibid* 103:249 (July 28) 1934) has reported the development of agranulocytic angina in a patient after ingestion of 21.8 Gm. (5½ drams) of 2,4-dinitrophenol sodium over a period of 4 months. The dosage was 4 mg. (1/16

grain) per kilo ( $2\frac{1}{5}$  lbs.) of body weight daily for 2 weeks and then doubled until the onset of unfavorable *reactions*. Treatment consisted of discontinuing the drug, administration of **pentnucleotide** and 1 **transfusion** of 250 c.c. of **whole blood**, following which, the patient recovered.

That the administration of *coal tars* in certain individuals produces changes in the blood picture characteristic of agranulocytosis is further emphasized in the report of a case by J. E. Benjamin and J. B. Biederman (*Ibid.* 103: 161 (July 21) 1934). The history is given with the comment that the granulopenia, at least in the case reported, was not of an atopic nature, but more in the nature of a drug hypersensitivity, with the hematopoietic system acting as the shock organ. This case responded favorably to high voltage **x-ray therapy**. During a period of good health the patient was given 10 grains (0.6 Gm.) of amidopyrine under control. This produced all the symptoms of agranulopenia within 48 hours. The administration of acetylsalicylic and allyl-iso-propyl-barbituric acids caused no unfavorable symptoms. Intracutaneous, patch and passive transfer tests gave negative reactions. In this patient the effect of amidopyrine was one of hypersensitivity to the drug and not, as has been mentioned, of an atopic nature.

The increase in the prevalence of granulocytopenia closely parallels the increase in the use of *amidopyrine*, according to L. F. Herz (*J. Lab. and Clin. Med.* 20: 33 (Oct.) 1934), who declares that inasmuch as the dangerous character of amidopyrine is established beyond any reasonable doubt, this drug should be strictly banned by the medical profession. Herz suggests the use of acetanilid as a safer drug when anodynes or antipyretics are indicated. An alternative but less efficient drug is acetphenetidin. By using the safer antipyretic, there is no doubt that greater efficiency will be obtained and granulocytopenia and other toxic phenomena now known to be caused by the dangerous pyrazolon group of drugs (amidopyrine and antipyrine) will be eliminated.

The relation of amidopyrine and the barbituric acid derivatives to granulocytopenia has been considered by the Council on Pharmacy and Chemistry of the American Medical Association in a report published in its official journal (*J. A. M. A.* 102: 2183 (June 30) 1934). The subject is reviewed at length, quoting practically all authentic workers. With reference to the etiologic aspects, several questions have been raised by these important contributions. Some of them, as stated in the special Council's report, are

1. Is amidopyrine primarily responsible for the production of granulocytopenia?
2. Are the barbiturates themselves important in the causation of this condition?
3. Are there any other predisposing, contributing, or specific factors involved in this disease?
4. Assuming that amidopyrine is an etiologic agent in granulocytopenia, is it necessary to stop its general use or to modify it, or do the conditions under which it is prescribed suggest that its relationship to granulocytopenia is within the realm of unavoidable accident and that any special caution may be disregarded?

The answers, contained in the Council's report, are quoted *verbatim*:

"As far as can be learned from the evidence at hand, there can be no question that amidopyrine is very important in the production of granulocytopenia. In fact no other agent has been found, either chemical or bacterial, which has been a factor in causing so many attacks.

"In the second place no definite case has been reported in which a barbiturate alone is responsible. From the present data it appears that barbiturates have little or nothing to do with granulocytopenia.

"There also is no doubt that many cases of granulocytopenia have occurred in which amidopyrine has never been taken, or any other drug, for that matter. One patient had 3 attacks. She never took drugs of any sort previous to the attack and during her last attack she received a sedative containing amidopyrine and she recovered promptly in spite of the constant administration of this drug throughout the acute phase of her illness. Moreover, it must be remembered that all patients who take or are given amidopyrine are suffering from some complaint or illness at the time the drug is being administered. There can be no question that fatigue and menstruation are important factors in inducing an attack quite apart from the drug therapy.

"When one considers the enormous amount of amidopyrine consumed and the relatively few individuals afflicted with granulocytopenia, it is obvious that one is dealing with a question of sensitivity in certain patients rather than with a universal action of the drug. In some respects it is analogous to the use of arsphenamines and the occasional occurrence of hepatitis or panmyelophthisis. It would be desirable to determine susceptibility in patients before amidopyrine is administered by the use of a test dose and a blood count, or perhaps by patch test, but it is apparent that such a procedure is impractical. Of course, if a patient complains of a rash, dizziness or a chill after amidopyrine is given, it should be discontinued. Probably the safest course to follow is to use another drug, such as acetylsalicylic acid, one of the barbiturates or codeine, if any of these are just as effective as amidopyrine for any particular symptom. If, however, amidopyrine is found to be unrivaled in its action for special complaint, it should not be administered for any great length of time, as a routine or in large doses unless white blood cell and differential counts are made at regular intervals. This is suggested, not because the occurrence of granulocytopenia is frequent, but because, when it does occur, it is an extremely serious accident. The indiscriminate and unnecessary administration of amidopyrine, and the self-administration by the public is certainly dangerous and should be discouraged."

**Diagnosis.**—The importance of the recognition of the early clinical aspects of agranulocytic angina is stressed by Burton (*loc cit.*) in order that the clinician may continuously be alert for its potential development. The distinctive points in diagnosis are fever, the septic lesion in the mouth or elsewhere, marked leukopenia associated with agranulocytopenia, no evidence of myelocytes, associated with slight or no affection of red blood cell or platelet. Subjectively, there are chill, depression, apprehension, prostration.

**Treatment.**—Emphasis is laid by Burton (*Ibid.*) on nucleotide treatment on the basis of the work done by Jackson and his associates. The mortality in

Jackson's report was the lowest of any published series of like size. The favorable clinical and hematologic response took place rather sharply about the fifth day of treatment, irrespective of how long the patient had been ill. The subsequent hematologic improvement in practically all cases followed the same orderly pattern.

The next choice in treatment is **blood transfusion**, in large numbers and in large amounts. Reznikoff has reported recovery of 11 patients in a series of 15 cases through administration of **adenine sulphate**. One gram (15 grains) of adenine sulphate boiled in 35 to 40 c.c. ( $1\frac{1}{8}$  to  $1\frac{1}{2}$  ounces) of saline, given warm, intravenously, 3 times a day, for at least 3 days for an adult, is nontoxic, and is suggested as the dose in treating agranulocytosis in adults.

**RETROPHARYNGEAL ABSCESS.—Complications.**—The subject of retropharyngeal abscess is discussed by L. Rosenberg and M. Berke (J. Pediat. 4: 764 (June) 1934), who list the complications in their main headings as follows: (1) death; (2) hemorrhage; (3) rupture of the abscess contents into neighboring parts; (4) general complications, such as facial paralysis, esophageal paralysis, pyemia, septicemia, thrombosis of internal jugular vein, pneumonia, lung abscess, edema of the glottis.

In puzzling cases of unexplained temperature in infants and children, despite the absence of suggestive symptoms of retropharyngeal abscess, digital examination of the throat should be made. To look at the throat is not sufficient. Because retropharyngeal abscess often goes undiagnosed and the patient is treated for other conditions, it does not necessarily follow that the mass found on digital examination of the throat has been present for a long period. The rapidity with which a cervical adenitis may show itself is familiar to all clinicians. Often overnight there may be marked enlargement of the gland. In the same manner, a retropharyngeal lymphadenitis, which has previously manifested itself by a slight boggy mass in the pharynx, may flare up in a period of from 24 to 48 hours to produce a true retropharyngeal swelling. For this reason a single, or even 2 or 3 consecutive daily examinations of the throat are not sufficient to exclude definitely retropharyngeal abscess. The throat must continue to be observed during the febrile period when the cervical adenitis persists and in certain cases even when it has greatly diminished in size or has disappeared. As great a source of error as any in the writers' experience has been the failure to consider seriously the presence of retropharyngeal abscess because of a subsiding cervical adenitis. Therefore, whether a large swelling of the cervical glands is present or not, the presence of temperature, not satisfactorily explained in a young child, is an indication for digital examination of the throat. It is important in such examination that the finger not only be carried down toward the glottis, but also upward to the posterior pharynx.

*Death* from retropharyngeal abscess has occurred from rupture of the abscess into the larynx and from hemorrhage from the carotid artery. Sudden death at the time of the incision, or shortly after, has been reported.

*Hemorrhage* complicating retropharyngeal abscess may be primary, before the incision is made, or secondary, following incision. Primary bleeding usually occurs in cases of longer standing, the time allowing for prolonged action of the

burrowing infection in the region of the carotid sheath. If the bleeding is severe and prolonged, it may result in collapse and death. Secondary bleeding is usually late in appearing, coming on several days after the incision, at a time when most of the danger is believed past. Several cases of recovery following **carotid ligation** have been reported. When severe hemorrhage occurs in the presence of retropharyngeal abscess before or after incision, ligation of the common carotid artery on the affected side should be done as an emergency measure. Even should the bleeding stop spontaneously, there is always the danger of recurrence, perhaps with a rapidly fatal outcome from exsanguination.

#### **FOREIGN BODIES IN HYPOPHARYNX AND ESOPHAGUS.—**

The value of radiography for the detection of foreign bodies of metallic density in the hypopharynx and esophagus has long been recognized. When, however, the foreign body is made up of small fish-bones or other objects causing little opacity, radiography is not appreciated to the same extent as a diagnostic aid. H. Carlsund (*Acta Radiol.* 14:391 (1933)) agrees with this, on the strength of his own experience, as far as the ordinary thread-like fish-bones are concerned, but he has submitted several cases to show that by the aid of an opaque medium (barium) it is possible to demonstrate bones of somewhat larger size, of flat or rod-like shape, although quite invisible to ordinary radiography and nonobstructive to the passage. The same holds good also for other bodies causing mild shadows of similar size.

In the cases described by the author the method of examination has been the usual one, using barium as the opaque medium in the form of thin porridge. The examination was carried out with the patient standing erect. Careful screening is necessary besides the taking of several separate pictures of parts suspected of holding some foreign body. It is also necessary, in taking several consecutive exposures, to let the patient swallow a little of the barium between each exposure. Small changes are of diagnostic value only if they constantly return on control radiograms, after further barium has been passed. In order not to overlook the smallest foreign bodies demonstrable by radiography, in the author's opinion, screening should be carried out and several radiograms should be taken, using different projections of suspicious parts of the hypopharynx-esophagus with the same care as is observed, for example, in the examination of the duodenal bulb when an ulcer is suspected.

A procedure which the author has made use of in the majority of examinations is to let the patient, after examination with barium, swallow a few mouthfuls of water. In so doing the hypopharynx and esophagus are washed clear of most of the barium, while some that has stuck to the foreign body or between this and the mucous membrane remains. In several cases the foreign body thus appeared much more distinctly than prior to water being taken, by virtue of its barium-coated surface in an otherwise washed-out hypopharynx-esophagus. In no case has the author so far seen all barium on the foreign body washed away by letting the patient drink a few mouthfuls of water. In some cases, the radiogram taken after rinsing with water was the decisive factor in arriving at the diagnosis. Out of 31 cases with positive x-ray findings of foreign bodies verified at subsequent esophagoscopy examination at the Sabbatsberg Hospital during 1930 and

1931, the method with taking water was used in 19 cases. Even in those cases in which the examination with barium gave no indication of any foreign body, the author generally finished off the examination by giving a few mouthfuls of water, in order to make certain that no trace of barium was left after washing down with water

**TONSILS, FUNCTION, INDICATIONS FOR AND RESULTS OF REMOVAL.**—The most important part of the treatment of heart disease, rheumatic fever, arthritis or chorea in children, states L. W. Dean (J. A. M. A. 103: 1044 (Oct. 6) 1934) is the eradication of chronic infection about the upper respiratory tract. It is axiomatic that the lymphoid masses in the throat, other than the palatine and pharyngeal tonsils, may be infected and consequently must receive attention in the control of the infection about the throat. It is also true that every vestige of infected lymphoid tissue cannot possibly be removed from the pharynx, but much more can be done than the removal of the faucial and pharyngeal tonsils. The course of the systemic response is an important factor in determining how thoroughly the work has been done.

The infection of the lymphoid masses of the pharynx is not the cause of rheumatic fever, heart disease, chorea or Still's disease. In toxic malnutrition secondary to infection of the lymphoid masses in the pharynx, the infection is the outstanding cause. A child with rheumatic fever and no infection about the upper respiratory tract may develop fever which can be controlled by the use of salicylates. The removal of the larger masses of lymphoid tissue in the pharynx early in childhood does decrease markedly the incidence of scarlet fever, common colds and otitis. The lymphoid masses of the pharynx have a decidedly important physiologic function. They should not be removed in children unless the deleterious results of the infected tonsils overbalance the good results of the physiologic action of these structures, or, the physiologic function has been so seriously interfered with by the infection that their defense reaction has been impaired or lost.

There is no agreement among physiologists as to the function of the tonsils. The tonsils, as well as other lymphoid structures, enlarge easily due to repeated infections, repeated colds, dietary disturbances, endocrine disturbances and toxemias. It is the opinion of the author that the tonsils in infancy and early childhood are a part of the defense mechanism of the body.

**Indications for Removal.**—Rules cannot be made to determine whether or not tonsils should be removed, according to Dean (*Ibid*). Each case presents its own problem. The result of removal in adults with chronic systemic diseases cannot definitely be predicted. In cases in which *infection of neighboring structures*, as the *middle ear, nasal sinuses and glands of the neck*, can be traced to infection of the tonsils, removal of the latter is indicated. The fact that a tonsil is chronically inflamed without any evidence of local or systemic disturbance is not sufficient reason for its removal, yet simple hypertrophy of the tonsils may demand their removal in order to get normal breathing.

The removal of macroscopically normal tonsils and hypertrophied tonsils with no evidence of infection has favorably influenced cases of *hemorrhagic nephritis, uveitis* or *rheumatic fever*. Microscopic examination of normal tonsils removed



because of a systemic disease, has shown, in every instance, chronic infection involving the epithelium deep down in the crypts. The evidence of infection found in the crypts is a leukocytic infiltration of the epithelium and underlying lymphoid tissue, with some destruction of the protective epithelium. In some cases in which the tonsils have been removed because of simple noninflammatory hypertrophy, such areas have not been found.

Two reasons for not removing the palatine tonsils under the age of 2 years are: (1) this is the age during which the tonsillar function is most important; (2) the operation at this age is more serious than later. If, however, there is a definite indication for the removal of the tonsils, it should be done. If an infant suffers from attacks of acute tonsillitis, and if with one attack it develops a lobar pneumonia which improves only with an improvement in the throat condition, it would be hazardous to leave the tonsils in. Adenoids blocking the nasopharynx may be removed at any age.

In a purely personal perusal of the results of tonsillectomy on private patients, M. H. Bass (*Laryngoscope* 44:780 (Oct.) 1934) found that the general result justified the operation in 133 cases out of a series of 150, was negative in 10 cases, and questionable in 7 instances. Of the 10 failures, 7 gave as the chief cause for operation, repeated colds; 1, anorexia and poor breathing; and 1, rheumatism and frequent colds; 1, unexplained fever. Of the total 150 cases, the following is the list of chief indications for operation: *colds*, 64, *tonsillitis*, 39; *vomiting*, 3; *sinusitis*, 2; *cervical adenitis*, 11; *rheumatism*, 2; *anorexia*, 8; *nasal obstruction*, 52; *otitis*, 18; *pyelitis*, 3; *unexplained fever*, 2; *croup*, 1; *deafness*, 1

The best results were obtained in cases of repeated tonsillitis or sore throat, in cervical adenitis and in otitis media. There was no appreciable difference in cases of sinusitis, before and after tonsillectomy, and, so far as nose colds are concerned, the operation is not of much benefit. In the rheumatic group of 10, only 3 were improved, while of the children developing permanent endocarditis, all 3 had had tonsils previously removed.

In the series of 150 cases, 6 cases required a second operation. One had had adenoidectomy only in infancy and had both tonsils and adenoids removed several years later. In the other 5, adenoid tissue had recurred. In *recurring hypertrophied adenoids* excellent results have followed **x-ray** treatment of the throat.

Finally, a careful analysis showed that where the greatest care was exercised in indication of operation and choice of operator, the child was distinctly benefited in 88 per cent of the cases. There is no question that even under these ideal conditions, accidents and serious sequelæ may occur, but in spite of these, with proper indication, tonsillectomy is a useful and necessary operation.

**CARCINOMA OF TONSILS.—Treatment.**—J. T. Dowling and M. F. Dwyer (*Ann Otol Rhin and Laryng.* 43:615 (June) 1934) review the subject, and quote, among others, Canuvt and Micaesco, to show that the tonsil is more frequently the seat of primary carcinoma than all the rest of the oropharynx. According to the authors, carcinoma of the tonsils is not a surgical condition and is best treated by **irradiation**. The interstitial implantation of platinum

filtered **radium** needles about the growth, the surface application of heavily filtered radium capsules to the lesion, and **x-ray** therapy externally is a very satisfactory method and in all probability the best method of dealing with this serious condition. Statistics show that approximately one-fourth of patients with carcinoma of the tonsils survive the 5-year period, but, in general, the prognosis is bad, especially when all cases are grouped in a statistical study.

The following operation for removal of carcinoma of the faucial tonsil and contiguous parts is suggested by D. Macpherson (*Ibid* 43:727 (Sept) 1934), who first tried the method on cadavers:

The external carotid artery is first tied, together with other important vessels, such as the ascending pharyngeal. After 2 weeks, the second stage is carried out. An incision is made from the symphysis of the inferior maxilla to the suprasternal notch, the lower extension being made lest the insertion of a tracheal tube should be considered necessary. The skin, superficial fascia and platysma of the affected side are reflected back without making lateral incisions. The corresponding half of the hyoid bone is uncovered and removed, leaving the periosteum attached to the uncut fibers of the muscles. The digastric attachment to the hyoid is separated and lifted upwards, as is the submaxillary gland. The mylohyoid muscle is separated from the attachment to its fellow of the opposite side in the median line and it, together with the geniohyoid, stylohyoid, middle constrictor, geniohyoglossus, mucous membrane, and possibly the hyoglossus, are severed laterally for a sufficient distance to permit of easy access and a good view of the lower pole of the tonsil and the surrounding area. Important structures brought into view and to be preserved during this phase of the operation are the hypoglossal, perhaps the glossopharyngeal and superior laryngeal nerves.

The diathermy cutting current was used almost exclusively, but the coagulating current was used to control the very slight hemorrhage. The upper pole of the tonsil, the involved palate and part of the base of the tongue may be reached and operated upon through the mouth. The external surface of the tonsils lies on the superior constrictors which separate them from the internal carotid arteries, internal jugular veins, pneumogastric nerves, etc., while the middle constrictors are in relation with the carotid vessels, the existence of which relationship must be borne in mind.

A feeding tube is placed in position through the nose. The hyoid muscles, upper and lower, are brought together and sutured, the external structures sutured and a drain placed in the lower angle of the wound. When healing takes place, deglutition and other functions of the hyoid muscles are not interfered with. The two-stage operation is done to protect the neck structures from mouth infections by new cicatricial tissue.

### LYMPHOEPITHELIOMA OF NASOPHARYNX AND TONSILS.

—In a study made by D. F. Cappell (*J. Path. and Bact.* 39:49 (July) 1934), 12 cases of malignant disease were included, which he believes are of epithelial origin, arising from the specialized epithelium of the pharyngeal lymphoid tissues. He emphasizes the value of silver impregnation of the reticulum as a means of demonstrating the structure of such growths. These tumors show distinctive clinical and pathologic features and may justifiably be separated from other neoplasms under the name of "*lymphoepithelioma*." Two main types of histologic structures have been recognized, one corresponding to the classic lymphoepithelioma of Regaud, and the other to the lymphoepithelioma of Schmincke. It is shown that these are not different types of neoplasm, but represent merely quantitative differences in the mode of growth and spread of the tumor cells. Evidence for regarding transitional cell carcinoma of the nasopharynx and the tonsil as a different form of neoplasm from lymphoepithelioma is not definitely established.

in the present observations, and it is believed that the two are at least closely related. Lymphoepitheliomas are highly radiosensitive, and the value of **radiation therapy** in contrast to surgical excision, is clearly demonstrated in the present series of cases.

**TUBERCULOSIS OF TONSILS.**—*Tonsillectomy in.*—The incidence and pathology of tuberculosis of the tonsils is discussed by H. Newhart, S. S. Cohen and C C Van Winkle (Ann. Otol, Rhin., and Laryng. 43:769 (Sept.) 1934). They believe that the highest percentage of favorable results in operating on pathologic tonsils in the tuberculous may be attained only by (1) a very careful selection of patients for operation; (2) by extreme care in employing an operative technic which will most effectively safeguard him from the possible complications; (3) by observing a carefully planned program for his after-care.

The incidence of tuberculosis of the tonsils in 112 adults studied by the authors was 42 per cent. If the 12 cases without pulmonary tuberculosis were eliminated, the incidence would increase to 48 per cent. Serial sections of the excised tonsils would materially increase the incidence. This was demonstrated by a study of 20 pairs of tonsils, in 4 of which tuberculosis was found. These had previously been reported negative by the usual microscopic study. In a control series of 100 routine tonsillectomies, the incidence was 1 per cent, the positive case being found in an individual who had previously been treated for active pulmonary tuberculosis.

In the opinion of the authors, the tonsils become infected by tubercle-laden sputum secondary to the open tuberculous pulmonary lesion. No case of primary tonsillar tuberculosis could be demonstrated in their series.

Tonsillectomy in the tuberculous, with the precautions cited, presents no special hazard which would justify failure to perform tonsillectomy when indicated.

E Schlittler (Schweiz med Wchnschr 64 594 (June 30) 1934) has revealed that in 98 patients with cervical lymphomas, suspected to be of a tuberculous character, but in whom pulmonary tuberculosis or tuberculosis of other organs could be excluded, the tonsils were removed and examination showed tuberculosis in 48 cases. Thus, it appears that in case of a prolonged lymphadenitis of the neck, particularly at the angle of the jaw, a primary tuberculous disease of the corresponding tonsil may be suspected, especially when in the region of the upper air and food passages there are no other causes detectable that would explain the swelling of the lymph nodes, and when the examination of the lung likewise remains negative.

In addition to the subacute or chronic form of lymphadenitis, there is also one in which an acute swelling of the cervical lymph nodes at the angle of the jaw becomes manifest with the symptoms of an acute tonsillitis or peritonsillitis. However, the stationary behavior differentiates it from the swellings of the lymph nodes caused by other infections. Schlittler believes that primary tuberculosis of the tonsil is not as rare. There is generally no macroscopic change in the tonsil and only microscopic examination permits a diagnosis. It is nevertheless advisable to remove the primary focus, the tonsils, for this measure would prevent a further invasion of tubercle bacilli from the tonsils into the cervical lymph

nodes and thus would lead to a more rapid cure of the tuberculosis of the cervical glands. The tonsils of these patients should always be subjected to microscopic examination in order to gain a better insight into the interrelation between primary tonsillar tuberculosis, tuberculosis of the lymph nodes and tuberculosis of the lungs. Physical and x-ray examination of the lungs should also be done.

**LINGUAL TONSILS.**—Some of the common abnormalities of the lingual tonsils are reviewed by L. Hollander (J. A. M. A 102:1151 (Apr 7) 1934), who attaches importance to these structures because a large part of the medical profession is not mindful of their existence. Although they may be involved in any one of what W. Boyd ("Surgical Pathology," p 436, Lea and Febiger, Philadelphia, 1933) calls the "big four" of pathologic changes of the tongue, *i. e.*, syphilis, carcinoma, tuberculosis and inflammation, they are much more frequently the seat of simple hypertrophy, residual infection or hyperkeratosis of the epidermis overlying them.

These simple conditions are frequently viewed with great alarm, as they are interpreted as malignant disease. Attention is usually called to them during routine examination of the throat or mouth. Subjective symptoms occur infrequently, and only when they are the seat of residual infection. Occasionally patients who are in the habit of looking at their tongues become aware of their presence and become greatly alarmed by finding these lesser or greater lumps.

As they are part of the lymphoid structure of the body, they are not infrequently found enlarged in patients in whom generalized lymphoid hypertrophy occurs. Or their crypts may be found to contain cheesy material which can be expressed. Subjective symptoms have also been noted in conjunction with lingual tonsillitis.

For *differential diagnosis* attention is directed by the author to (1) The absence of (a) hardness, as in carcinoma, (b) progressive or retrogressive changing character, as in a syphilitic gumma, (c) satellite lymph node enlargement, as in a chancre, (d) slow progressive ulceration quality, as in tuberculosis.

The *treatment* is best carried out with the **radio knife**, performing **excision** under local anesthesia.

**NOSE AND NASAL ACCESSORY SINUSES.—COMMON COLD.**—*Etiology.*—An attempt to analyze the *weather conditions* in relation to common cold has been published by M. Gover, L. J. Reed and S. D. Collins (Pub. Health Rep 49:811 (July 13) 1934). They state, "Because summer and winter, in terms of meteorological conditions, are a composite expression of many varying factors, the problem of relating the incidence of disease to atmospheric conditions is a complicated one. It is obvious that the mere increase in mortality in the fall and winter when there is a decrease in the hours of sunshine cannot be assumed to express any causative relationship. The same is true of temperature and other weather conditions that may, on closer examination, be found to be associated with the incidence of respiratory diseases. Aside from the fallacy of assuming causative relationship, it cannot be assumed that there is any very close association between such variables as respiratory disease incidence and temperature or hours of sunshine until the usual or normal seasonal variation has

been eliminated from the picture. So many weather conditions show the same seasonal swing that any one or all might appear to be closely correlated with respiratory affections unless examined apart from seasonal variation."

The data used in this study were obtained from a survey made on the weekly incidence of respiratory disorders among students in various universities of the United States in a period of 18 months from November, 1923, to April, 1925. The 6 university groups comprising the study were distributed geographically: Boston; Washington, D. C.; Columbus, Ohio; Chicago; New Orleans; and Berkeley, Calif. Weather conditions with respect to mean temperature, daily temperature range, relative humidity, absolute humidity, hours of sunshine, wind velocity, precipitation, and the respiratory attacks, were considered in weekly intervals. A full 12 months period was also presented to give a climatic background for each city. An examination of the weather variables by statistical methods did not reveal any close association between the magnitude of the respiratory attack rate and weather conditions, though there was a tendency to slight association of some of the items. Thus, for the year ended May 2, 1925, in each city except Boston, the attack rate showed a small negative correlation with the mean temperature. This appears to be statistically significant as judged by its probable error. Daily temperature range, however, showed a significant correlation in only one of the cities. It was concluded that no definite association of respiratory attack rates with marked variations in climate could be determined. Weekly deviations from the "norm" of the respiratory attack showed a small association with deviations from the "norm" in mean temperature for the corresponding week and also for the preceding week. A respiratory attack rate above normal was associated with a mean temperature below normal; this association was higher during the early fall months than at any other time of the year.

It has been difficult to collect reliable information of the incidence of respiratory disturbances in relation to weather conditions on a large number of persons to have significance. Climatic and geographic distribution has also been difficult to obtain, but, as the most extensive study so far made on the subject, the report of Gover and her collaborators offers some corroboratory basis for the common impression that "colds" are more frequent in cold weather

In discussing the *common cold in infancy*, J. Brenneman (Illinois M. J. 66:366 (Oct.) 1934) states that it is difficult to know where the common cold ends and where other things that are much worse than the ordinary common cold begin, *e. g.*, sore throats, tonsillitis, etc. It is a common experience to see in the same family a father with, perhaps, a common cold which the mother acquires as a result of contact, one of the children may develop glands in the neck or an adenitis and possibly another one will develop one of those more serious conditions that, if not scientifically accurate, will perhaps be called the "real flu" or grippé. As a matter of fact, they doubtless all have the same etiology and clinical significance, except that there is a different manifestation in the various members of the family.

**EPISTAXIS.—Treatment.**—The submucous injection of sclerosing solutions for the control of recurrent epistaxis is preferred by some rhinologists to

other methods. The technic as used by N. Asherson (J. Laryng. and Otol. 49: 180 (Mar.) 1934) is as follows:

A 2- to 5-c.c. record syringe with an angled bayonet-fitting needle is used, such as is used for injecting a local anesthetic preliminary to a submucous resection of the septum. A 10 per cent. **phenol in almond oil solution** is injected. The septal area is blanched and anesthetized by applying to each side a plug of cotton wool saturated with 10 per cent **cocaine** and **adrenalin**. Any excess is expressed from the plug before insertion, to avoid swallowing of the toxic substance. The plug is left *in situ* for 10 minutes. The tortuous, dilated venules are frequently thrown into relief against a pale background of blanched mucosa. A point is noted, as low down as possible,  $\frac{1}{4}$  to  $\frac{1}{2}$  inch in front of the bleeding area, *c. g.*, where a vertical, tortuous, dilated venule is observed running to the area. A drop of pure **carbolic acid** at the end of a tuft of wool is applied to this point through which the bleeding area is to be infiltrated. The needle is inserted through this normal area to undermine the mucosa and the bleeding area, and the solution is slowly injected. The effect is rapidly observed by the blanching of the venules. The needle is withdrawn and re-inserted, if necessary, so as to inject the entire field. About 0.5 c.c. (8 mmims) is injected in each side. A tuft of cotton wool is left in each nare. There are no untoward after-effects. The method has been used in children and adults.

**ERYSIPELAS.—Complications.**—*Necrotizing ulcers* complicating erysipelas have been described by P. F. Stookey, C. R. Ferris, H. M. Parker, L. A. Scarpellino and K. E. English (J. A. M. A. 103: 903 (Sept. 22) 1934). Five cases are discussed in which the ulcers were confined to the edematous loose areolar tissue about the eyes. The distinguishing characteristics of the ulcers were their rapid development, phagedenic properties, punched-out appearance, edematous base and profuse, creamy, yellow discharge. Two of the 5 cases proved fatal. The rapidly necrotizing character of the ulcers and the persistent finding of staphylococci, both by culture and by smear, suggested a superimposed infection from a skin contaminant developing on a suitable nidus. The organism was recognized to be a staphylococcus by its morphologic and cultural characteristics.

**FRACTURE OF NASAL BONES.**—In the present day machine age there has been a great increase in the number of injuries involving the head and face, and especially is this true of fractures of the facial bones. According to W. G. Gill (South. M. J. 27: 197 (Mar.) 1934), most fractures involving the facial bones, except those of the nasal bones, extend into one or more of the paranasal sinuses, and fractures involving the wall of the orbit are often complicated by involvement of the adjacent paranasal sinuses. Surgical shock is always an accompaniment of the more severe fractures of the facial bones.

Where communication with the nose or sinuses has been established, air may easily find its way into the soft parts and emphysema is likely to occur, especially in fractures involving the medial wall of the orbit or the anterior wall of the antrum. Emphysema is less frequently encountered following fractures involving the frontal sinuses, but it does occur.

Displacement of fragments or hemorrhage into the orbit may seriously interfere with motility of the eyeball or be responsible for its actual displacement.

Pressure from massive hemorrhage into the orbit has been known to result in atrophy of the optic nerve. Hemorrhage and emphysema may occur simultaneously in the soft parts.

Fractures involving the *maxillary sinuses* or *antrum of Highmore* are quite frequent, because of the fact that the malar bone is, next to the nasal bones, the facial bone most frequently involved in fractures, and because of the fact that this bone forms a large part of the lateral and superior walls of the antrum.

Fractures of the *frontal sinus* are especially serious, because of the likelihood of injury to the brain or meninges. The anterior or posterior wall of the frontal sinus may be involved alone or in combination.

Fractures involving the *ethmoidal sinuses* are usually caused by some penetrating object, although they may occur if fracture lines radiate from contiguous bones. The essential features are epistaxis and emphysema of the orbital tissues. Meningitis may follow fractures in this region, and is especially likely to occur if the cribriform plate of the ethmoid bone is involved. Cerebral rhinorrhea, which is almost invariably fatal, may be a sequel to such fractures.

**Diagnosis.**—The **x-ray** is not as valuable in diagnosing such fractures as it is in other parts of the body. Inspection and palpation of the underlying bony parts and comparison with the opposite side will often reveal a fracture with displacement of the fragments, where the x-ray has failed to reveal it. Certain radiographic signs have been described by J. J. Shea (J. A. M. A. 96:418 (Feb 7) 1931) which are of value in diagnosing fractures of the facial bones, especially the malar bone. These signs are based on alteration in the relationship of two lines visible at the lateral margin of the orbit in an anteroposterior film taken in the position usually employed for maxillary sinus x-rays. The same writer considers a change in the transverse diameter of the orbit of definite diagnostic value in such injuries.

**Treatment**—It is essential that fractures involving the facial bones be reduced as quickly as possible. Oftentimes swelling of the overlying tissues or infiltration with blood makes it necessary to postpone reposition of the fragments for several days, because of the fact that palpation cannot be accurately employed through swollen tissues to determine when reduction has been effected. A variety of methods may be used to reduce the displaced fragments.

In the treatment of fractures involving only the anterior wall of the *frontal sinus*, it is best to **remove loose fragments** of bone, close the overlying skin and provide for **endonasal drainage**. Particular care must be exercised to determine whether the posterior wall is injured. When the inner wall of the frontal sinus is fractured, it is imperative that **external drainage** be provided to prevent accumulation of pus under pressure. Infection may follow fracture lines and involve neighboring structures. If the posterior wall is fractured, then external drainage must be provided and great care exercised to see that the cavity is not infected during the convalescent stage, as pathogenic bacteria easily gain access to the sinus through the nasofrontal duct.

In fractures of the *ethmoidal* or *sphenoidal sinuses* the treatment resolves itself into keeping the nose free from infection, preventing adhesions, and avoid-

ing emphysema of the surrounding soft parts by abstaining from forcible blowing of the nose.

*Prolonged suppuration* following injury to any of the sinuses may necessitate operative **exploration of the sinus** or removal of an offending foreign body, or sequestrum. Persisting infection in any of the sinuses will render the prognosis more serious in adjacent fractures. Where there is great edema of the soft parts, it is best to delay reduction of the fragments until the edema has subsided. Reduction may be accomplished satisfactorily 2 weeks or even longer in certain cases. Union is, however, quite rapid in facial bone fractures. Fortunately, many such injuries are seen before edema comes on and it is at this time that reduction can be accomplished under the most favorable circumstances, provided shock does not interfere.

Because of the fact that many of these injuries are incurred on highways, tetanus is to be considered and a prophylactic injection of **tetanus antitoxin** is advisable in all fractures of the nasal bones associated with open wounds. Most fractures about the orbit and paranasal sinuses may be reduced under **local or general anesthesia**. In several instances in patients with depressed fractures of the malar bone, the author infiltrated the fracture line with 1 per cent **novocaine solution** and effected reduction without discomfort to the patient. Massive infiltration with the anesthetic solution should be avoided, as it will interfere somewhat with palpation of the underlying fragments, making it more difficult to determine when reduction is complete. This is not a serious objection and should not act as a deterrent so far as the use of local anesthesia is concerned. Where local anesthesia is not considered practicable, the usual **gas-oxygen** anesthesia is entirely satisfactory for the average injury.

In the treatment of fractured *nasal bones*, A. B. K. Watkins (Brit. M. J. 2:905 (Nov.) 1933) describes a method based on a **splint** described by Carter. The author first modified the splint by substituting U-shaped metal splints for Carter's straight intranasal splints, one limb of the splint being inserted so that, when traction is taken from the part of the limb outside the nose opposite the middle of the nasal bone, the effect is the same as if short intranasal splints were used and traction were taken from the middle of them. In order that the splint should not work in farther or work out when tension is applied, it is found essential that such tension should be applied exactly at right angles to the axis of the nasal bone. This is obtained by adding a mast, the effective length of which can be varied, from the forehead to the apex of the splint. Grooves are cut on the mast and a silk thread from each U splint is tied to its fellow of the opposite side over the correct groove in the mast in such a way that the direction of the pull is at right angles to the nasal bones. The bases of the splint are fitted with thick rubber tubing and are used only for counterpressure on the face. When wounds are present, they are avoided by adjusting the distance between these rubbers with a milled screw. If, during treatment, the silk threads need only slight tightening, this is effected by adjusting the screw to narrow the angle between the two sides of the splint. The forehead piece of the splint is padded with a flat piece of rubber and kept in place with a band of adhesive strapping around the head. Nasal respiration is possible during treatment. The splint is



left in about 4 days, though at any time it may be removed (all except the mast) for the dressing of wounds and the use of douches, and it can readily be reapplied. Adjustments may be slackened after this period and recurrence of deformity watched for. If none occurs, the splint is removed; otherwise, it is replaced. Treatment varies from a few days up to about 3 weeks.

**GRANULOMATOUS ULCERATION.**—This disorder of the nose is described by J. P. Stewart (J. Laryng. and Otol. 48:657 (Oct.) 1933). In his opinion the most descriptive term is "progressive lethal granulomatous ulceration of the nose." He reviews 10 cases. The disease is practically confined to the male sex, the ratio being 9:1. Eight of the 10 cases occurred between the ages of 28 and 42 years. From the clinical and microscopic appearances, the author concludes that the disease is not one of tumor, but essentially a pyogenic one, a chronic inflammatory process. The clinical picture is one of progressive destruction of the nose, face and pharynx.

The disease is characterized by a mild leukocytosis (14,800) or a leukopenia (2200), with the white blood cells in their normal proportions. There is a prolonged and hectic fever and frequent, severe hemorrhages. The duration of the illness is from 1 to 2 years. The most marked feature is the patient's complete absence of resistance to the infection. The disease must be differentiated from ulceration occurring in the nose due to syphilis, tuberculosis, malignant disorders, agranulocytosis, mycosis and myiasis, yaws, leprosy, rhinoscleroma, leishmaniasis, rhinopharyngitis mutilans (gangosa) and trophic postencephalitic ulceration. In 6 of 7 cases in which bacteriologic observations were made, the presence of a streptococcus in combination with a staphylococcus was reported.

Local applications proved unavailing. Radium treatment was employed in 2 cases with indefinite results, but **high voltage x-ray therapy** promises more success and deserves further trial. Eight patients died from the direct effects of the disease. sapremic cachexia and repeated hemorrhage. One survived for 4 months after local cure before succumbing to generalized sarcomatosis cutis and 1 died from atypical "miner's phthisis" 4 years after recovery from the local disorder.

**ALLERGY.**—*Cytology in.*—In commenting on the cytology of the secretions in allergy of the nose and paranasal sinuses, F. K. Hansel (J. Allergy 5 357 (May) 1934) states that in the various shock organs or tissues in which the lesions of allergy occurs, the pathologic picture is characterized by edema and eosinophile infiltration. In the nasal, paranasal sinus, bronchial, conjunctival, intestinal and genitourinary tissues, the eosinophiles migrate through the epithelium and may be found in the secretions. The demonstration of these cells in the secretions, therefore, may be utilized as a means of corroborating the diagnosis of allergy.

In the collection of secretion from the nose for smear examination, several methods may be employed. Specimens should be taken separately from each side of the nose. Secretion is most easily and readily collected by having the patient blow the nose on a waxed paper or cellophane handkerchief. This gives a specimen which represents only nasal secretion or a collection of both nasal and sinus secretion. If no secretion is available from blowing the nose, it may be

necessary to remove it by swabbing with a cotton applicator. Secretion may also be collected in a specimen bottle at the time of an acute exacerbation. The insertion of a saline tampon into the nose may stimulate the flow of secretion so that sufficient material may be obtained. Secretion from the individual sinuses may be obtained by aspiration or by puncture and washing. Gross masses of secretion may be used for smears or the returned fluid may be centrifuged if no gross mass of material is available.

In the *collection of secretion* for examination, it must be taken into consideration that great variations may occur as to the quantity and quality of the material available. Patients usually report for examination during or immediately after an exacerbation of symptoms. During the periods of reactions the secretion may be thin and watery, with very little if any mucus present. Thin, watery material may show eosinophiles only after many examinations. Often they are found clumped in small masses or clusters. If mucoid material is obtained, an abundance of eosinophiles may be found. The histopathologic examination of the mucous membrane shows the maximum infiltration of the eosinophiles just beneath the basement membrane. From here they migrate through the basement membrane and the epithelium to the surface, where they are uniformly distributed. They are then collected in the mucous secretion, which is rolled or propelled toward the nasopharynx by ciliary action. In this way the cells are collected in great numbers in the mucus. Watery secretion usually flows very freely and does not collect the cells as does the mucus. If the mucoid secretion should be very profuse, fewer cells may be found. Sometimes collections of mucus show very few if any cells. If it should happen that some material which had been immediately secreted from a gland be collected, the cellular content may be very scarce, because the eosinophiles do not migrate through the glands to any appreciable degree. Immediately following a period of reaction and during the quiescent stage which may immediately follow, an abundance of thick mucus may be found collected in the nasal cavity, just as it collects in the bronchi after an exacerbation of asthma. This secretion usually contains an abundance of eosinophiles. During quiescent periods, however, the nose may be dry with very little if any secretion available for satisfactory examination. With the cotton applicator sufficient material may be obtained. Small bead-like masses may be found, which represent clusters of desquamated epithelial cells. Eosinophiles may or may not be found in them. Hansel summarizes as follows:

- 1 The demonstration of eosinophiles in the secretions from the nose and paranasal sinuses is good presumptive evidence of the existence of allergy.
- 2 The presence of neutrophils in the secretions in addition to eosinophiles is an indication of the existence of superimposed infection.
- 3 The eosinophilic-neutrophilic proportions are an index of the nature of the infection.
- 4 By repeated observations on the cytology of the secretions, acute and chronic infections can be differentiated.
5. A pure eosinophilic response as the result of bacterial hypersensitiveness is not definitely substantiated on the basis of clinical evidence.

6. Cases of hyperplasia and polyposis with a persistent absence of a diagnostic number of eosinophiles, as a rule, do not prove to be allergic.

**ALLERGIC RHINITIS.—Treatment.**—Nasal pathology as a nonspecific factor in the treatment of inhalant allergy is commented upon by W. T. Vaughan (Virginia M Monthly 60: 598 (Jan.) 1934). Definite conclusions regarding the incidence of *sinusitis complicating asthma* in children cannot be drawn, since the figures obtained by various investigators are so diverse. The reported incidence in 3 available reports range from 6 to 100 per cent. He quotes R. A. Kern and J. C. Donnelly (J Allergy 3: 172 (Jan.) 1932) on 200 asthmatics and 50 so-called normal controls. The latter were non-allergic individuals in the same age brackets and living in the same districts. Eighty and five-tenths per cent. of the asthmatics showed x-ray evidence of sinus disease, and 72 per cent. of the "normal controls" showed similar findings. Kern and Donnelly also observed that the average number of sinuses affected per patient was 4.14 for the asthmatics and 3.9 for the non-allergics. Their observations give some justification to the conclusion that the incidence of sinus infection is slightly greater among chronic asthmatics than among non-allergic individuals, and that this infection, when present, is likely to be somewhat more diffuse. The difference, however, is not great. These authors found that the incidence of x-ray evidence of sinus infection is the same in non-allergic controls and in individuals with seasonal hay fever or asthma. The percentage in the former was 72 and in the latter, 74.4. Again, Kern and Donnelly found that in seasonal hay fever and asthma, just as good results were obtained from **specific treatment** alone in those cases with sinus disease as in those without. The presence of sinus infection, untreated, in no way interfered with good specific results.

The author states that sinus infection complicating an extrinsic allergy should, therefore, not be submitted to surgery until after specific therapy has had a very thorough trial. In 55 to 65 per cent. of all asthma and vasomotor rhinitis cases, the nasal pathology is not the cause and its removal will not influence the results as long as the extrinsic allergen is still active. However, **obstructive nasal pathology should be removed** to promote ventilation, and an outspoken active sinus infection will require treatment irrespective of any possible connection with the allergic state. In his series, allergic therapy was successful in but 35 per cent. of those cases showing nasal pathology who had previously been subjected to surgery. The results were much better (59 per cent.) in those showing nasal pathology which had not been treated surgically. But best results were obtained (68 per cent.) in those without nasal pathology.

In the nasal treatment of hay fever, C. Frances (Practitioner 132: 529 (May) 1934) uses light **intranasal cauterization**. The procedure is as follows. A small swab of absorbent cotton is twisted on the end of a probe, dipped in a 10 per cent. solution of **cocaine hydrochloride** and wrung out almost dry. The interior of the nose is examined, and the septum and the inferior and middle turbinates are touched lightly in rotation with the swab. The most sensitive areas are anesthetized by painting them 3 or 4 times with the solution. The areas should be touched lightly with a fine cautery point heated to a dull red, the heat being turned off just before the cautery point is applied. One or more light

longitudinal burns should be made, when necessary, on the septum and inferior turbinate, and a few light touches on the anterior edge of the middle turbinate. The marks produced by the cautery should be nearly or entirely gone in a week or 10 days. If necessary, a second application is made to any remaining hypersensitive areas. There is no pain, swelling of the parts or sloughing, and no after-treatment is required. Of the 100 cases treated by the author in this way, 74 patients obtained complete or great relief, moderate relief was evident in 24, and 4 obtained either slight relief or none.

H. L. Warwick (*Laryngoscope* 44:173 (Mar.) 1934) discusses the treatment of hay fever and its allied conditions by **ionization**. He includes in his report only those cases which have been entirely relieved of their symptoms for more than 1 year. All of the patients reported had hay fever as their major allergic manifestation, but 10 of the cases were complicated with other manifestations of the disease. Four patients suffered from asthma in addition to hay fever, and 6 had perennial hyperesthetic rhinitis. All but one of the patients have been entirely relieved of symptoms for more than a year, and 19 of them for more than 3 years.

Thirty-one in this group of 40 patients required only 1 ionization for complete relief, 7 required 2 ionizations, and in one it was necessary to repeat the ionization the third time before permanent relief from symptoms was obtained. (One case was entirely relieved of symptoms for 1 year, then returned and was given 2 more ionizations without any relief whatsoever. All but 8 of these patients had had the sensitization tests and in 14 there were other positive reactions present in addition to the autumnal pollens. Several patients had, in addition to the hay fever, food sensitivities and the majority of these patients after ionization apparently lost their sensitivity to these foods because contact with them no longer produced nasal symptoms. Eight of the total group had received no treatment whatsoever for either the hay fever or the other symptoms, while 32 had had all sorts of therapy, including the desensitization by vaccines, local treatment and nasal operations, without relief. Warwick concludes that ionization of the nasal mucosa, using a zinc, cadmium and tin electrode and salts of the above solutions in the electrolyte, produces a chemical change in the patient ionized which renders him less sensitive to substances to which he previously gave definite allergic manifestation.

**Radium** in the treatment of various forms of nasal disease other than malignancy has proven to be of value. L. B. Bernheimer and Max Cutler (*Arch Otolaryng* 17:658 (May) 1933) reported the effect of irradiation on the allergic nasal mucous membrane of 40 patients having *hyperesthetic rhinitis*. All the patients treated gave a typical history of spasmodic attacks of sneezing followed by profuse watery discharge and nasal blockage, the symptoms occurring without relationship to season or climate. Eleven of the patients had demonstrated sensitization to one or more foods or inhalants and none had responded to allergic therapy. No patient was irradiated in the presence of polypi or secondary nasal infection. The treatment consisted of introducing 50 mg. of radium into each nasal chamber and allowing it to remain in place for a total of 200 mg. hours. After one year, 52 per cent. of the patients were symptom-free, 20 per cent. no

longer had nasal blockage or watery discharge, so that while sneezing still persisted in a moderate degree, from the standpoint of the patient's comfort, the clinical result was excellent; 8 per cent. were moderately comfortable; 10 per cent. received only little benefit, and 10 per cent. were not benefited.

**INTUMESCENT RHINITIS.**—*Treatment.*—The use of **sclerosing injections** in the treatment of varicose veins also finds an application in the treatment of congestive rhinitis, according to M. Bruker (*Ann d'oto-laryng.*, p. 1107 (Oct.) 1932). The solution employed is 80 per cent. neutral **glycerin** in distilled water, put up in 3-c.c. ampoules. The injection is carried out through a wide bore needle fitted into a Luer syringe. After local anesthesia of the inferior turbinate, the liquid is slowly injected deeply into the mucous membrane from behind forwards. Some pain is produced which lasts a few seconds. This can, however, be avoided by a preliminary injection of **novocaine** or by the use of a more dilute solution of **glycerin**, 50 or 60 per cent. Following the injection, the nasal fossa is lightly plugged with ribbon gauze, partly to seal the puncture opening made by the wide bore needle, and partly to arrest hemorrhage.

When the operation is completed, the lining membrane of the turbinate looks pale and edematous and there will be some temporary hydrorrhea and nasal obstruction. The injection should be repeated between the third and fifth days, as the first injection produces only a sensitization of the tissues. As this sensitization takes some time to establish itself, there should always be an interval of 1 to 6 days between the injections.

**RHINITIS.**—*Treatment.*—**Zinc ionization** in various forms of rhinitis is rapidly becoming an established procedure. Since best results are obtained in limited disorders of the nasal mucosa, the indications for its use must be clearly understood. A. R. Hollender (*Arch. Phys. Therapy* 15:581 (Oct.) 1934) in more than 1000 ionization treatments during the past 10 years, obtained good results in *simple chronic rhinitis*, so-called *intumescent* or *mild hypertrophic rhinitis*, and in *mild involvements of the anterior ethmoidal sinuses*. It was also shown to be a valuable postoperative aid, especially when healing of the nasal membranes is for some reason delayed. He believes that ionization of the antral mucosa is indicated after window resection when resolution does not occur as promptly as it should from a simple drainage. Zinc ionization minimizes and frequently cures postnasal discharge when the source is strictly localized in the nasal mucosa.

The process of ionization as now employed therapeutically must be considered as capable only of a superficial action on open surfaces and mucous membranes. The older belief that it is possible to "drive in" drugs into the tissues through the skin is too fallacious for scientific consideration. In ionization of mucous membranes, tissue change is stimulated. It is quite likely that this change involves surface tissue penetration of an electrolytic substance. The depth of penetration of the various ions depends on several factors. Estimation of the quantity of an ion that will be introduced in any given period requires consideration of the electrochemical equivalent. This is the quantity, by weight, which is liberated by 1 ampere for 1 second, and this weight is in proportion to the chemical equivalents of the ions.

The action of zinc ions on the mucous membranes differs from that of the medicinal ions. In the case of the latter, a soluble molecule is absorbed by the tissues, while in the former an insoluble precipitate is produced in the tissues. It is claimed that the effect of this precipitate is sterilizing or germicidal, depending upon the milliamperage or strength of the current and the duration of the flow. During each treatment, the patient experiences a pronounced metallic taste and a profuse salivation. After the treatment, a grayish surface discoloration of the mucous membrane is observed. This is probably a mild surface coagulation, as the discoloration cannot be removed easily by rubbing. When seen on the day following the treatment, the nose is usually obstructed with a white or grayish membrane which is quite adherent to the mucosa. This membrane is not disturbed until the third day, when, if it is still present, it may be removed. After the mucous secretions again become stimulated, the mucosa is gradually restored to its original color. In addition to the local reaction, all the symptoms of an acute coryza appear and persist for 1 to 3 days.

The simplest *technic* and one which operates satisfactorily in any cavity has been extensively employed by A. R. Hollender (*loc cit*, p 623) as follows

It consists of packing the nasal chamber with long, narrow strips of gauze well moistened with zinc solution (Friel's formula) **zinc sulphate** 5 Gm ( $1\frac{1}{4}$  dram), **glycerin** 60 c.c (2 ounces), with water to make up 1000 c.c (1 quart). For treatment this solution is diluted with an equal amount of warm water. Caution should be used in covering all surfaces by introducing the gauze firmly high up, posteriorly, and in the middle and inferior meati. Before the treatment is started, the membranes should be cleansed of secretions and crusts by suction, tampons, or irrigation with the same zinc solution used to moisten the gauze packing. *Anesthesia* is obtained by using 2 per cent **cocaine solution** applied on pledgets of cotton and left in place for several minutes. The negative pole, which is a felt pad of about 5 x 7 inches, may be fastened around the forearm, or preferably to the nape of the neck. The patient is placed in a reclining position, with the head somewhat lower than the rest of the body. An insulated wire with a zinc fixation electrode is attached to the wet packing and held in position by some dry cotton packed into the meatus. This wire leads to the positive pole of a galvanic generator set or battery. Another insulated wire connects the moistened felt pad to the negative pole. With this arrangement the circuit is completed. The current is turned on very gradually and increased until the patient develops a metallic taste and profuse salivation. When the point of comfortable tolerance is reached, the current strength is maintained. If the meter indicates that the tolerance is at 10 ma, the treatment is continued for 15 minutes, if the reading shows 15 ma, the treatment is discontinued after 10 minutes. In the case of children and some adults, with a tolerance of about 5 ma, the current should be maintained for 30 minutes. The plan is to give 150 ma minutes, arrived at by multiplying the current strength in milliamperes by the minutes during which the treatment is continued. The suggested durations of treatments are rather arbitrarily based on experience, but a reasonable extension will occasionally prove of benefit. In fact, improved results were noted in many instances when the fixed treatment was even doubled.

**POLYPI.**—The **postoperative use of radium** in the treatment of nasal polypi is described by Walter A. Ford (Wisconsin M. J. 32: 824 (Dec.) 1933). The surgical removal of all visible polypoid material continues to be the first step in the treatment. On the thoroughness with which the polypi are removed depends, to a large extent, the results which will be achieved. As pointed out, the use of radium will have no influence on the polypus itself, and it is this fact that has led some to the conclusion that radium is of no value in these cases.

Not only must the polypi be as thoroughly removed as possible, but the diseased bone must also be removed if at all practical. Where the polypi and their underlying diseased structures can be reached, as in the maxillary antrum, using the Caldwell-Luc operation, it is believed that radium is seldom necessary. At first, radium was used postoperatively on nearly all types of polyp cases. The author, however, now limits its use to only those cases involving the ethmoid cells, anterior and posterior. These are the cases which are of the recurrent proliferative type, most difficult to deal with surgically. In some of his earlier cases, Ford waited a week before applying radium. He found that it could be used just as well within 48 hours.

There is a marked difference in the penetration of the beta and gamma rays of radium. The ordinary metal container or tube used in cavity work will screen off most of the less penetrating or soft beta rays. "The hard rays are of extreme tenacity and it is doubtful if 1 cm. of lead will completely block them" (Newcomet). "To get deeper effects, the greater quantity of beta rays are cut off so that only gamma rays are employed. In such cases thicker filters are necessary. Two mm of platinum or 4 of lead or silver cut off practically all of the beta rays" (Knox). An account must also be taken of the moist character of the parts being treated. A dosage causing some discomfort if applied to dry skin will not have this effect in the nose.

The question of the exact amount of filtration in any case where radium is used is of paramount importance. The author first used 25 mg of radium on each side for 45 minutes. Monel metal tubes or needles of 0.4 mm. thickness were employed. Radium sulphate is inclosed in platinum cells of about 0.1 mm thickness within these needles. One layer of dental rubber is wrapped around the needles after anchor strings are attached and the whole is then covered with a light layer of absorbent cotton for insertion into the diseased area. The dosage has been increased in most cases from 38 to 100 mg hrs without disagreeable symptoms. This treatment is repeated every 2 or 3 weeks, until from 3 to 8 treatments have been given. Should polypi recur during this time, they are removed and more radium used.

**SINUSITIS.—Treatment.**—Each case of chronic sinus disease must be dealt with as an entity. Repeated failures of cure of sinus disease are too frequently interpreted as indicating improper diagnoses. The use of **autogenous vaccines** in the hands of some rhinologists have proven to be of value. W. C. Cox (Mil Surgeon 73:117 (Sept.) 1933) has had 28 patients suffering from chronic sinusitis, nasal allergy or asthma of the bacterial type under autogenous vaccine treatment. The patient was skin-tested by injecting 0.05 cc of the various skin test emulsions intradermally in the inner surface of the forearm. Reactions were read in 1 hour and in 24 hours. The formation of a characteristic wheal or the formation of a red tender area 1.5 cm. or more in diameter, was considered a positive reaction. With the use of 0.05 cc of a 500,000,000 suspension, the patient received approximately 25,000,000 organisms as a skin test dose. Emulsions of the organisms that gave positive skin tests were used in preparation of the autogenous vaccine. The individual emulsions were standardized at 1,000,000,000, through the use of a 0.25 per cent solution of phenosaline

as a diluent and a 1,000,000,000 MacFarland standard. Equal portions of each of the emulsions were mixed in a 50-c c sterile vaccine bottle and tested aerobically and anaerobically for sterility.

The initial *dose* of vaccine was 0.05 c c, injected intracutaneously. Reactions were carefully noted and a subsequent increase or decrease of the dose made. Injections were given every fourth day, each dose being increased by 0.05 c c until 0.3 c c was given. Following this, each dose was increased 0.1 c c and the injections were given subcutaneously. The maximal dose used was 1 c c. This dose was continued until examination revealed marked improvement in the mucous membranes of the structures involved, in addition to subjective improvement, or until failure of the vaccine was indicated. Of the 28 patients, 71.4 per cent. were so improved as to be classed as cured.

*Immunization*—A new method for the treatment of chronic sinus infections is recommended by F. C. Kracaw (California and West Med. 40:228 (Apr.) 1934). The procedure devised by A. P. Krueger (J. Infect. Dis. 53:237 (Sept.-Oct.) 1933) for local and general immunization seemed particularly well suited to this end. Cultures are taken in the usual fashion from the nasal tract and are immediately seeded into broth and brain suspension media. After a short period of incubation, the tubes are plated out on whole-blood agar and chocolate agar, from these plates the pathogenic forms are isolated. Mass cultures are grown, harvested in Locke's solution of pH 7.0, and are thoroughly washed in several changes of the solution. The cells are then disrupted in a special ball mill and the suspension is filtered through acetic collodion ultrafilters. The essential points in this technic are

1. Exclusion of metabolites by means of thorough washing of the cells before maceration.
2. Avoidance of alterations in the cellular antigens by exclusion of heat or chemical treatment.
3. Removal of viable bacterial cells with the ultrafilters.
4. Standardization of the solutions on the basis of nitrogen content.

Local immunization or desensitization is accomplished by direct application to the diseased tissues. At the same time, general systemic treatment is carried on with intradermal and subcutaneous injections.

*Dosage and Administration*—For the past year the writer has used the following procedure in administering the treatment. Beginning with the weaker solution, the antigen is administered hypodermatically 3 times weekly, the first dose being 0.1 c c intradermally, and 0.1 c c subcutaneously. It has been found more satisfactory to make these injections in 2 separate areas, 2 or 3 inches apart. The intradermal dose remains the same throughout the treatment, while the subcutaneous dose is raised as rapidly as possible to the maximum, usually from 0.5 to 0.8 c c. Four or 5 maximum doses of this weaker solution are given. Care should be exercised always to remain just below the reaction dosage. Reactions are rarely encountered and are never severe, but it is felt that treatment is more satisfactory when they are avoided entirely. The stronger solution is now substituted and the same procedure followed. The entire course requires 10 to 14 weeks to complete.



A fixed scale of dosage, applicable to all patients, has not been found feasible. Increase or decrease must be regulated with each patient, according to the subjective general and objective nasal symptoms presented. The writer has found that an increase of 0.1 c.c. in each successive subcutaneous dose represents the usual limit of tolerance without reaction. Care should be taken not to exceed the maintenance dose, which has been found to be just below the reaction dosage.

The lysate is administered simultaneously with the antigen by local application to the nose and sinuses about every fourth to sixth day. Where the posterior series of sinuses are involved, it has been the author's practice to give the nasal mucous membranes a preliminary shrinking with **cocaine** and **adrenalin**, then to fill the sinuses by the Proetz displacement method. The antra are more satisfactorily reached by direct injection through the normal openings, through windows if present, or by puncture beneath the inferior turbinate.

Some local reaction may be expected following the first 3 or 4 nasal applications, usually manifesting itself by a mild degree of nasal obstruction, and possibly by a slight headache, which may persist for an hour or so. In many cases it has been found advantageous to add a few drops of 3 per cent. aqueous solution of **ephedrine** to the lysate just before instilling. However, a few patients may be encountered who will present a typical ephedrine reaction when this is done.

Since the first response of the tissues to this treatment is phagocytic in nature, one of the early signs of favorable reaction will be an increase in the amount of discharge from the sinuses and a change to a definitely purulent character of discharge, even though originally it may have been mucous or mucopurulent in character. This discharge soon becomes clearer and gradually begins to disappear.

An analysis of the end-results in 45 cases treated by this method shows satisfactory improvement in 95 per cent, and marked improvement or cure in 66 per cent.

However, **surgery** in the treatment of chronic sinus disease where osteitis and mucous membrane changes are present remains the method of choice.

The *preturbinate route to the maxillary sinus* is preferred by many surgeons, and is successful only if free drainage is established and all diseased membrane removed. This can only be accomplished when the whole of the maxillary sinus cavity is visible. The Caldwell-Luc technic is, perhaps, used more extensively than the preturbinate route because of easy access and clear vision of the interior of the sinus. The dangers of loss of sensation of the teeth in the region of the incision and injury to the infraorbital nerve must be considered. The vertical, instead of the horizontal incision, has been advocated to obviate this injury to the dental nerves. Here again, free ventilation and drainage must be established, and all the lining membrane must be removed. There must be nothing in the nasal passage to obstruct drainage or ventilation, and portions of the middle and inferior turbinate bodies must be removed if indicated.

*Tamponage and Diathermy*—This has been found by J. N. Fishbein (Rhode Island M. J. 16: 179 (Dec.) 1933) to be the most effective method of treatment. The **colloidal silver solution** employed passes through the membrane without ill effects and is capable of destroying bacterial life without injury to the tissues.

Leaving the tampons in place for about an hour enhances the use of diathermy and the time of treatment is reduced to about 15 or 20 minutes. The tampon is saturated with the colloidal silver solution and inserted into the middle meatus as far back as possible in the direction of the sphenoid sinus. Preceding this, a smaller tampon is inserted high into the olfactory fissure. The indifferent or dispersive electrode is placed on the forehead by means of a head-band. The electrode consists of a piece of block tin about  $1\frac{1}{2}$  by 6 inches. The two ends of the diathermy tape from the nostrils are attached to one of the poles, and the tape from the dispersive electrode to the other terminal. A current of from 250 to 450 ma is employed and left on for about 20 minutes. Many conditions, such as acute or chronic infections of the nasal accessory sinuses, are benefited. When the patient is found to be hypersensitive to some dust or food, an attempt is made at desensitization to the specific substance. When no specific substance is found, nonspecific treatment is given, consisting of the **parenteral injection of a nonspecific protein**.

**SINUSITIS IN CHILDREN.**—Sinus disease now ranks as one of the most common disorders of childhood. R. Ashley (California and West Med 40. 156 (Mar.) 1934) states that interference with free nasal ventilation and drainage is the basic predisposing factor; endocrine disorders, metabolic disturbances, and lowered resistance from improper diet favor a general predisposition.

The immediate *etiologic factors* are acute infection of the respiratory tract, common colds, the acute exanthemata, especially pertussis and measles. Poor living conditions, including food, vitamins, clothing, housing, climate, swimming and diving and contact with other infected persons likewise contribute.

Some of the more common *symptoms* of sinus infection are acute and chronic pharyngitis, laryngitis and bronchitis, with hypertrophy of the lymphoid follicles of the posterior pharyngeal wall, cervical adenitis; enlarged peribronchial lymph nodes and peribronchial thickening, bronchiectasis, frequent head colds and recurrent epistaxis, fits of sneezing, chronic cough (especially at night), attacks of croup, otitis media, headaches, fever without apparent cause, conjunctivitis, orbital cellulitis; orbital abscess, optic neuritis, keratitis, iritis, and blinking of the eyes.

*Systemic complications* may include anemia, malnutrition, asthma, gastrointestinal upsets, tubular and granular nephritis, pyelitis, myocarditis, chorea, acute rheumatic fever, arthritis, meningitis, cavernous sinus thrombosis, and brain abscess.

**Treatment.**—The treatment of sinusitis in children is more difficult than in adults. Variations in anatomy and symptomatology require the soundest judgment in determining whether treatment shall be medical alone or combined with surgery, as well as the type and extent of surgical procedures. Treatment according to the following outline has led to the best results.

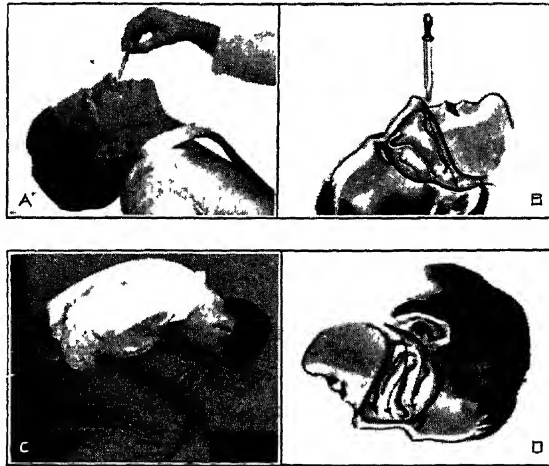
- 1 The sinuses are involved in all common colds and should be treated to prevent the disease from becoming chronic.

- 2 The **diet** should be regulated and corrected as far as possible. Milk, cream, butter, eggs, vegetables and fruits in unrestricted amounts, and whole-

wheat cereals in moderate amounts should be given. Other carbohydrates should be limited.

3. In allergic states, an effort should be made to identify the allergen and eliminate it.

4. Internal medication. In acute cases small doses of **atropine sulphate** at 3- to 6-hour intervals, and in older children, capsules containing **atropine sulphate**, **luminal**, **ephedrine sulphate** are given. **Calcium gluconate** and **parathyroid** are often beneficial. **Thyroid** in small doses is indicated if hypothyroidism is present. **Cod-liver** or **haliver oil**, given 3 times a day, is valuable. **Autogenous** and **stock vaccines** frequently give good results.



**Beck's Postural Method of Treatment**—In this method the head is tilted back. One-half dropperful of the solution is instilled in each nostril (*Figs A and B*). The head is immediately thrown forward, which allows the medication to come in contact with a larger surface of the nasal mucosa (*Figs C and D*). The solution introduced with a medicine dropper falls into the inferior meatus, backward, until it strikes the nasopharyngeal wall. Allowed to remain in this position, the solution then runs down into the nasopharynx. As the head is thrown forward, the solution strikes the posterior nasopharyngeal wall, and at least some of the solution is returned through the middle and superior meati, allowing it to come in contact with the openings of the anterior ethmoid sinus, maxillary sinuses, and frontal sinus.

5 Other general methods include **quartz light** treatment over the entire body daily; elimination of swimming and diving; **strenuous outdoor exercise**, followed by a **shower** or **tepid sponge**; warm sleeping quarters during acute attacks, and isolation from other infected members of the family.

*Local treatment* consists in shrinking the nasal mucous membrane with **adrenalin** or **ephedrine** preparations followed by packing the nose with cotton saturated with one of the **silver preparations** such as 20 per cent **solargentum**. This medication may be used in the home in the form of drops instilled into the nose as shown in the following illustration.

**MAXILLARY SINUS.—Anatomy.**—The shape, size, position, variation and measurements of the maxillary sinus in a representative group of roentgenograms of both sexes of various ages were studied by H. J. Sedwick (*Am. J. Roentgenol.* 32:145 (Aug.) 1934). He observed that the maxillary sinus varies greatly in shape, size and position, not only in different persons, but in each side of the same person. The sinus reaches its maximal size during the third

decade of life and does not increase thereafter. In the later decades there is a definite tendency toward the assumption of the triangular form. When the sinus is triangular, the position of its base varies. The relation between the floor of the sinus and that of the nasal cavity varies and is not a characteristic of sex. The sinus is in close proximity to the sides of the nasal cavity. The only difference between the sinuses in the white and the Indian skulls examined is that the vertical height is less in the Indians, a fact that might be correlated with the shorter nose and broader cheeks of the race. The average measurements for the sinus, based on 173 cases or 346 sinuses, are height 34 mm, width 25 mm, and anteroposterior length 39 mm. The average maximal and minimal measurements are height, maximal 46 mm, minimal 22 mm, width, maximal 35 mm, minimal 17 mm, anteroposterior length, maximal 51 mm, minimal 29 mm. The average height for men is 35 mm and for women 34 mm. The average width for men is 25 mm and for women 24 mm. The average length for both men and women is 40 mm.

**SPHENOIDAL SINUS.**—The advisability of opening the sphenoidal sinus when only few and vague symptoms are obtainable to justify the operative procedure instead of the positive objective or visual justification of empyema and pus, is discussed by R. F. Ridpath (*Laryngoscope* 44: 657 (Aug.) 1934). He states that it is not so difficult to visualize a virulent infection of a mucous membrane with its consequential swelling, to understand the closure of a small ostium, which, when due to the circulation, consumes all oxygen in the cavity. Here there is a typical and idealistic condition for the growth of cultures and bacteria organisms whose requirements for oxygen are *nil* and knowledge of medicine and bacteriology is of decided usefulness in remembrances of infections of the most virulent character, which are of anaerobic origin. Should an example be necessary, the resultant ravages with tetanic infections may be recalled. To make the necessary examination requires time, patience and persistency, all of these to be augmented with the scientific and personal desire to arrive at a truthfully correct diagnosis.

The first essential is to examine all parts of the nose, making a mental or written note as to the conditions found. Next, the mucosa should be shrunk with a weak **cocaine solution**, waiting until the shrinking is complete, which requires fully 10 minutes. A second examination should be made, with the touching up with a stronger cocaine solution (5 or 10 per cent) of various areas which have not responded to the first solution. It will also be advantageous to apply this stronger solution between the middle turbinate and septum and anterior wall of the sphenoid. Adrenalin or other drugs of this character should not be used in making the examination. While waiting for a complete cocaineization, a careful postrhinoscopic examination should be made, as well as the condition of the mouth, tonsillar areas and larynx noted. Attention is called to the fact that in some cases of postnasal dripping the pus may and does lodge in the pyriform sinus, with resultant ulcerations, fistula formation or a perichondritis.

When cocaineization is complete, the pharyngoscope is used and, either with this means or by the use of the Skillern probe, the ostium of the sinus is found. As before stated, the deeper the sphenothmoidal recess, the more external the

ostium will be located. It will frequently be necessary to bend the probe at an angle to enter those so located. When this is done, a bead of white pus may be seen by the aid of a pharyngoscope placed in the other nostril and directed to the examined side; drainage continuing along the shaft of the probe. In other cases, those of an anaerobic nature, as soon as the probe enters the sinus cavity, a slight noise may be heard by the patient and doctor, caused by the inrush of air into the cavity, with sometimes an immediate cessation of all symptoms.

Knowing the position of the ostium, the sinus can now be irrigated, the patient holding the head forward to prevent the lavaged material from going down the throat. Should an x-ray study be made, it can be done at this time with either the silver probe left in the sinus or a radiopaque oil injected into the cavity.

**Complications.**—Ridpath (*loc cit.*) further states that due to the intimate anatomical relation between the sphenoid and cavernous sinuses, the latter may become readily infected. *Retrobular neuritis*, with sequela of partial or complete loss of vision, is a complication too frequently met. *Basal meningitis* is observed more frequently than *thrombosis of the cavernous sinus* and the author has never seen a case, whatever the treatment may have been, get well.

*Meningitis* in relation to pathological conditions of the sphenoid is discussed by W. P. Eagleton (Tr. Am. Laryng. Rhin. and Otol. Soc. 38:51, 1932). He draws his conclusions from a series of 112 postmortems of meningitis and states that:

1. When pneumococcic meningitis follows a cold in the head, the sphenoid should be suspected of being the primary focus of the meningitis, provided, of course, that no other infection, such as pneumococcic otitis or a pneumonia, was present prior to the original headache.

2. The presence of a positive blood culture in a pneumococcic meningitis without thrombophlebitis of one of the large venous sinuses adjacent to the ear should awaken the suspicion that the sphenoid may be the primary focus of infection.

3. Pneumococci have a selective affinity for damaged cerebral tissues and for the blood vessels of the choroid plexus and the ependyma.

4. In meningitis with streptococcus blood infection without venous sinus thrombosis, there is apt to be present a suppurative focus in a medullary bone adjacent to the meninges. This is frequently the petrous apex where it abuts into the sphenoid.

5. In meningitis of blood stream origin from suppuration of the sphenoid, the temporal bone connected with the ear opposite to the discharging or paining ear is often more seriously affected than the side which is discharging or which has caused pain.

*Carotid ligation* possibly acts by the control of venous stasis of the cortical and ventricular veins, which is an outstanding postmortem finding in all cases dying of subacute meningitis.

**EAR.—CHOLESTEATOMA.—Etiology.**—A clinical analysis of 50 cases of chronic suppurative otitis media with cholesteatoma is presented by M. Day (Arch. Otolaryng. 20:602 (Oct.) 1934). *Moisture* is the primary and major factor in the development of cholesteatoma. Only anhydrous solutions should be employed in the presence of cholesteatoma. Conservative treatment should be tried only in the absence of symptoms or signs of extension beyond the confines of the middle ear and mastoid. A cure can be obtained only if there

is complete epidermization of the walls of the cavities. The presence of moisture will prevent cure and cause recurrences. This is especially true if granulations or an open Eustachian tube is present.

**Pathogenesis.**—The pathogenesis of the “genuine” cholesteatomas is considered by K. Wittmaack (Arch. f. Ohren-, Nasen- u. Kehlkopfh. 137:306, 1933), who follows W. Albrecht (Acta oto-laryng. 15:375, 1931), in distinguishing between secondary or pseudocholesteatomas, which develop after otitis media, and the genuine, spontaneous, or primary cholesteatomas. With slight modifications he accepts, also, Albrecht’s theory that the latter are essentially congenital dermoid-like tumors. He considers chiefly the primary cholesteatomas which invade the middle ear, and which can often be distinguished from the secondary type at operation or, in some instances, only at necropsy.

In general, primary cholesteatoma is distinguished by the fact that the ingrowth of squamous epithelium occurs in the pars flaccida or Shrapnell membrane, not in the pars tensa, of the tympanum, and that inflammation and suppuration are secondary events. Since the primary form is much more dangerous because prone to lead to serious or even fatal complications, radical operation is invariably indicated.

**Symptoms.**—The clinical symptoms and therapy of cholesteatoma of the middle ear were studied by L. Ruedi (Schweiz. med. Wchnschr. 64:411 (May 12) 1934) in 763 cases of chronic suppuration, in the course of 14 years. In 762 cases, a peripheral, epitympanic perforation of the ear-drum was found to be the point of origin of the cholesteatoma (in one case only, a centrally located perforation), corresponding to the genesis of the cholesteatoma from epidermis of the external auditory meatus, which grows into the epitympanic space of the middle ear through the peripheral perforation. In about one-third of the cases, the peripheral defect of the ear-drum arose in the course of an acute otitis with measles, scarlet fever, diphtheria, etc., or as the result of a tuberculous suppuration of the middle ear. With the latter, along with complete defects, multiple perforations are frequent.

**Complications.** Cholesteatomata with large defects of the ear-drum are somewhat more frequently complicated by *suppuration of the mastoid process* and *paralysis of the facial nerve* than those with smaller perforations, according to Ruedi (*Ibid.*), whereas *endocranial complications* (extradural abscess, meningitis, cerebral abscess) are more frequent with the smaller perforations. Therefore, a conclusion may be drawn more or less as to the type of complication threatened from the location and size of the perforation.

**Treatment.**—Especially the *cholesteatomata with small perforations* are unsuitable for conservative therapy, but a preventive **radical operation** is indicated, according to Ruedi (*Ibid.*), in view of their tendency to dangerous complications, even without acute symptoms, especially when the patient is irregular in coming for treatment or when frequent or stubborn relapses occur in spite of conscientious irrigation. As the ear-drum in these cases is preserved in large part, the radical operation may be as conservative as possible. With this in view, 342 of the 763 cases were operated radically. Only 3 of those operated

required subsequent operation because of relapse. Thanks to this active procedure, there was a mortality of only 1.18 per cent. for the 763 cases.

Conservative treatment is rarely successful in young children, according to Day (*loc. cit.*), because of tubal secretion. Periodic examinations are important after the ear has become dry. The early recognition and proper treatment of chronic otitic suppuration with cholesteatoma should obviate the need of radical operation and prevent the serious complications which so commonly occur at present.

The author reported a total number of 50 cases. In 14 of these he performed a **radical operation** on the mastoid. In 10 of the 14 there was extension of the infection to the dura or labyrinth. In 37 cases **conservative treatment** was used, with a dry ear resulting in 31, or 84 per cent. The conservative treatment consisted of: (a) providing **free drainage**, as by **removing polyps** or **granulations**, (b) removing the cholesteatoma by **lavage**, using only 95 per cent. **alcohol** or **ether**, followed by **suction**, and (c) having the patient use drops of 95 per cent **alcohol** at home.

**DEAFNESS.—Etiology.**—A study of the distribution of ages of children who have registered in 16 American Schools for the deaf indicated to F Heider (Am. J. Hyg 19:756 (May) 1934) that there was a relationship between the *influenza* epidemic of 1918 and deafness. Birth dates were obtained from these schools of 7247 white children. C. E. A. Winslow stated: "Having had the opportunity of reading Dr. Heider's paper, I have been greatly impressed with its significance. Otitis media was a rare sequel of the 1918 influenza epidemic in the north and though its presence was noted in one or two southern camps no discussion of the subject has, to my knowledge, ever assigned any importance to this complication. A psychologist working a Massachusetts school for the deaf had in 1933 discovered and demonstrated beyond question the existence in the southern states in 1918 of a secondary invader which had a far-reaching influence in producing deafness in infants suffering from influenza." Such a revelation of an important epidemiological factor, unsuspected by those working with the disease at the time, constitutes a truly dramatic incident in the history of vital statistics." Heider's statistics indicated that the peak of mortality of the influenza epidemic came in October, 1918, one month later than the peak of the birth cure for deaf children. The sharp rise and fall of the birth cure suggests that the effect on hearing, insofar as it was general enough to show in a broad statistical study, occurred only in children who were less than 4 months old at the time of the epidemic.

Based on a statistical study, G. E. Shambaugh, Jr. (Ann Otol, Rhin and Laryng 43:513 (June) 1934) states that profound deafness in childhood is half congenital and half acquired. Treatment cannot improve the hearing, but many of the acquired cases should be prevented by protecting young children from the acute infectious diseases. Mild deafness in childhood is usually due to catarrhal otitis media and can be relieved by treatment. Mild degrees of deafness in adult life may be the residue of childhood tubal catarrh. This type of defect is not progressive. Active tubal occlusion occasionally occurs in adult life and can be relieved by treatment. Chronic running ears account for 10 per cent. of

severe adult deafness and this 10 per cent is largely preventable by early and adequate treatment. Chronic aural discharge should always receive treatment until the ears are dry. Otosclerosis causes 70 per cent. of severe adult deafness and can neither be prevented nor helped in the present state of knowledge.

Deafness, according to E. P. Fowler (*Ibid*, p 387), that occurs in individuals over 50 possibly indicates *cardiovascular disease*. He reports that through audiometric tests by air and by bone conduction, he is able to show that deafness in the majority of cases increases with frequency of arteriosclerosis and age of the patient. In 90 per cent. of 167 pairs of ears examined, he found either identical or similar graphs for both ears in each case, indicating that the etiology was the same for both. Eliminating other factors, Fowler holds that similar lesions in the inner ear or high acoustic tracts are the logical explanation for similar bilateral losses of hearing by air and bone conduction, and that in patients over 50 years old, audiometric tests showing losses of hearing, especially in the higher frequencies, are suggestive of cardiovascular disease, usually arteriosclerosis. Not air conduction, but bone conduction tests are what impress Fowler, since bone conduction measurements check the nerve apparatus functioning, and "show a more orderly ratio of progress at the different frequencies with advancing age." Autopsy findings were correlated with clinical findings, and indicated that arteriolar sclerosis could be expected to loom up more often in the internal auditory meatus than in the modiolus. The prime lesion, he claims, is degeneration of the ganglion cells and their terminal fibers in the spiral lamina's lower turns.

Concluding, Fowler holds that audiometric measurements on the one hand, often aid in the diagnosis of general or cardiovascular disease, which may be "the most important factor in the etiology of nerve deafness", and on the other hand, may be used in known arteriosclerosis cases as an aid in determining rate of progress of the disease.

**Deafness, Blue Sclerotics and Fragile Bones.**—In a communication containing the report of a case, J. Dessoff (Arch Ophth 12 60 (July) 1934) discusses this very interesting triad from a historical and clinical point of view. *Heredity* is a prominent feature of the disease and while it is most prevalent in females (55.4 per cent.), it may be transmitted by either group, being only transmitted by parents to children and never skipping a generation. It is warned that those of this group who marry have a 50 per cent. chance of transmitting the condition. The blueness of the sclera is a very striking characteristic. This blueness of the eye is present at birth and remains practically unchanged throughout life. It is generally agreed that the blueness is not scleral, but is a choroidal pigmentation seen through a transparent sclera.

The most serious clinical feature of the disease is the liability to fracture from inadequate causes (60 per cent. have this tendency). Usually healing is rapid and is contrary to a desire on the part of clinicians to feed calcium in such cases when there is no such deficiency. The fractures occur most frequently in childhood and have a tendency to diminish as the patients pass puberty. Deafness, the third feature of the disease, occurs in about 60 per cent., most fre-



quently after the age of 20. This deafness is usually attributed to otosclerosis, occasionally complicated by labyrinthine disease and nerve deafness.

Dessoiff reviews the various theories as to the etiology of the disease, with the strong possibility that *hyperparathyroidism* may be the cause. Drugs, chemotherapy, vitamins, diet, irradiation and endocrine preparations have been tried but no form of treatment is known to have any effect upon this condition.

**Diagnosis.**—The detection of simulated deafness is discussed by R. D. Russell (*Laryngoscope* 44:201 (Mar.) 1934), who stresses the importance of ruling out those who feign a loss of hearing, either as a hysterical manifestation or malingering. There may be no actual defect in hearing acuity or there may be an exaggeration of an actual defect. There is great difficulty in evaluating simulating bilateral deafness, but fortunately the defect is usually unilateral. The approach of the examiner must be sympathetic, in order to throw the malingerer off his guard. It is also important not to tell the patient why he is suspected of being a malingerer, because actually he learns by each examination and may even avail himself of standard texts (to say nothing of being coached by unscrupulous professionals). The patients' reactions must be carefully observed. The malingerer makes exaggerated attempts to hear, while the truly deaf individual makes no great effort to hear. In voice tests the malingerer repeats words which have no similarity in sound to those spoken by the examiner, while the truly deafened person responds with words of similar sound to those spoken by the examiner. The malingerer is frequently antagonistic to the examiner, but the truly deafened is very rarely so. As was just stated, each time an intelligent malingerer is examined, he learns something about the tests, and to warn the otologist against instructing these malingerers, by letting them know by either word or manner at which point they have been detected. On the contrary, a few more tests should be done after detection, in order that the malingerer shall not suspect just what response trapped him. The examiner must be careful not to stigmatize a patient as a malingerer on mere suspicion. Then, too, the fact that the examiner is convinced that a patient is malingering is not sufficient, for many of these cases are potential court cases, and the otologist must be prepared to defend his opinion on the witness stand.

**Treatment.**—The otologic management of progressive deafness, according to G. M. Coates and W. Gordon (*Tr. Am. Acad. Ophth.*, 1933) is divided into 3 fundamental principles: (1) The institution of measures calculated to prevent deafness, (2) measures that will aid in the conservation of hearing, (3) careful testing of the functional capacity of the acoustic apparatus from time to time.

**Preventive Measures.**—Every otologic case should be thoroughly studied. A careful history, a general examination, and a thorough local examination may lay the foundation for the institution of proper therapy. The family history of deafness should be carefully inquired into, for where a hereditary factor exists, the acoustic apparatus of such an individual already is a "*locus minoris resistentiæ*," more vulnerable to deleterious influences than a normal acoustic mechanism would be. Syphilis hereditary or acquired, acute contagious diseases, the exanthemata, all upper respiratory infections, poor health habits, metabolic faults, nutritional imbalance, endocrine imbalances, the intermarriage of persons with a family

history of deafness, the harmful effect of noise upon the delicate organ of Corti, harmful drugs, such as arsenicals, quinine and salicylates (on the perceptive apparatus), swimming, diving, improper nose blowing, middle ear suppurations, infection of the nasal accessory sinuses, infections in remote parts of the body, such as those in the gastrointestinal or genitourinary tract, dental infections, these are some of the influences.

In brief, Coates and Gordon have reason to believe that they have found, chiefly, multiple foci of infection situated in the nose, throat, mouth and distant foci, besides extraneous environmental conditions, to account for the deafness. It remains for the otologist to search carefully, systematically and thoroughly for every possible cause with a view of removing that cause. By removing the cause the effect may be prevented.

*Conservation of Hearing*—All measures designed for the prevention of deafness constitute the first and basic principle of conservation of hearing. When the causative factor has been removed, the perceptive apparatus begins to show improvement, provided that it has not suffered irreparable damage. The question of local measures is considered by the authors with the old axiom, "a thousand men, a thousand minds," holding true. They sound a keynote of warning against indiscriminate removal of diseased foci as well as haphazard unconsidered surgery. **Inflation of the Eustachian tube** is described in detail by blowing medicated vapor into the tube. E. Simon (*Ann Otol, Rhin and Laryng* 43: 598 (June) 1934) uses **heat bougies** in treating Eustachian tube obstruction. He varies the procedure at different times, but essentially it is the insertion of the bougie through a short (Yankauer) catheter and then turning on of the heat gradually at the rheostat dial until the galvanometer of the thermocouple reads 110° F (43.3° C). This temperature is maintained for a period of 10 minutes, following which the heat is completely turned off but the bougie is still left in the tube. After 10 minutes the bougie is withdrawn. The procedure was usually done weekly.

The patient is warned against improper blowing of the nose and taught to blow with both nostrils wide open. Where aural suppuration is present, every medical and surgical effort should be made to get the ear dry. According to Coates and Gordon, it is of the utmost importance to conserve the hearing in infancy and childhood, so that the integrity of the acoustic apparatus may be retained to an efficient degree throughout life. Since they believe many cases of progressive deafness in adults are an aftermath of inflammatory states of the Eustachian tube and middle ear in infancy and childhood, the closest cooperation between pediatrician and aurist is necessary in all cases of contagious diseases, acute exanthemata and respiratory diseases. The children should be frequently examined. During acute attacks of any *upper respiratory infection*, careful attention should be directed to the nose and nasopharynx, **mild shrinking solutions, warm alkaline solutions**, and any form of **colloidal silver** may be **instilled in the nose** with a medicine dropper, or a **mild shrinking solution**, followed by very **gentle glass suction**, followed by a **bland oil** will be found efficacious.

*Recurrent attacks of upper respiratory infections* can be curtailed by a surgical cleanup of the nasopharynx, *i. e.*, **removal of the pharyngeal tonsil** as well as the **degenerated lymphoid tissue** in and around Rosenmueller's fossa. After any upper respiratory infection has well subsided, it is important to ventilate the middle ear cavity and invigorate the drumhead by **gentle inflation** with either a **Politzer bag** or a **nebulizer** for a number of treatments, as well as to **massage the drum and pinna**.

When deafness supervenes, suitable cleanup and local measures should be instituted, and all hygienic measures utilized. Where the deafness is incurable, suitable **hearing aids** should be recommended, the study of lip or speech reading urged and the attendance upon hard of hearing clubs advised. The aurist should never relax in his endeavors to keep up the courage, morale and spirit of the deaf one. From time to time, thorough functional testing of the acoustic apparatus should be performed, utilizing all the standard tests, in order to know the progress of the disease.

The *results of treatment* in syphilitic involvement of the eighth nerve were given by A. Ciocco and A. Weinstein (Am. J. M. Sc 187:100 (Jan.) 1934). They examined by means of audiometers the ears of 286luetics who had no middle ear infections nor had suffered hearing defects before they acquired syphilis. The tests were on hearing by air conduction, since shortened bone conduction (in the presence of otherwise good hearing) was not observed except in cases of high-tone loss. Of the 286luetics, they found one-third had diminished vestibular reactions unaccompanied by any impairment in hearing; but of those who did hear poorly, one-half exhibited diminution of the vestibular reaction. Their statistical studies caused them to conclude that (1) just because aluetic's hearing has faltered badly is not sufficient reason to conclude that he has arrived at the stage of neurosyphilis, though it is true that involvement of the eighth nerve is associated with neurosyphilis more than with other forms (2) Anti-syphilitic treatment has no effect, neither beneficial nor detrimental, on hearing (with the exception of improving deafness associated with early meningeal neurosyphilis). However, Ciocco and Weinstein could detect no relationship between the amount of antisiphilitic treatment received and the development of hearing defects. In fact, they otologically reexamined 61 patients 2 years later only to discover that hearing remained stationary in 52, improved in 4 and became worse in 5. The 2 showing most improvement had early meningeal neurosyphilis (neurorecurrence), the 2 with greatest decrease had late syphilis.

**EAR AND SWIMMING.**—A. Werner (Schweiz Med Wchnschr 64 418 (May 12) 1934) shows that the drowning of the person who does not swim differs from the drowning of swimmers, the latter occurrence being designated as sinking. Whereas, in the persons who do not swim death is caused by suffocation because of the inability to keep above water and to breathe, the cause of the sinking of swimmers lies in the body itself. The sinking of a swimmer generally takes place without a struggle as the result of partial or total loss of consciousness. The author states that laymen generally ascribe the sinking of a swimmer to loss of movement, to "spasm," but he points out that there are several other possibilities. Ulrich advanced the theory that the main cause of

the sinking of swimmers is digestion hyperemia, and the author decided to investigate this theory in postmortem examinations on 50 drowned persons, of whom 27 had died while swimming. In about 70 per cent of these, digestive hyperemia occasionally combined with other factors, was the cause of death; 10 per cent had severe cardiac and vascular disturbances, and it may be assumed that they sank because of sudden death in the water; while 20 per cent had no digestive hyperemia but had mild cardiovascular disturbances or other anomalies. In the latter group, various causes may have caused death. In 32 cases the petrous bones were examined in order to determine whether the sinking was the result of otogenous factors. The author believes that otogenous drowning is comparatively rare. He believes that the possibility of this mode of death can be conceded in only 1 of the 32 cases examined for this cause. Approximately 90 per cent of the swimmers who died sinking had slight or no hemorrhages in the middle ear. Such changes were most frequent in the nonswimmers who drowned.

The author gives the following warnings to bathing or swimming persons: (1) It is dangerous to bathe or swim while the stomach is filled, for digestion hyperemia is one of the main causes of death. (2) Weak and hypersensitive persons, and particularly those with heart disease must be especially cautious. (3) Patients with disease of the middle ear should be aware of the fact that the entrance of cold water into the ear irritates the labyrinth, causes vertigo and may lead to drowning.

W. Schmid (*loc. cit.*) states that the managements of swimming pools warn persons with defective tympanic membranes against diving. The author relates the histories of 3 persons in whom a rupture of the tympanic membrane occurred while diving. In discussing these cases he shows that not only perforated tympanic membranes deserve attention, but abnormally thin membranes and those with atrophic scars likewise present a grave danger. For this reason the examining otologist should search for perforations and should examine the mobility of even apparently normal tympanic membranes by means of Siegle's speculum. Moreover, even in the case of an apparently normal tympanic membrane the diver should be advised to protect the ears against the force of the water.

**HERPES ZOSTER OTICUS—Pathogenesis.**—Inasmuch as many otitic and intracranial conditions are simulated by the various manifestations of herpes zoster oticus, R. A. Fenton (*J. A. M. A.* 103:468 (Aug. 18) 1934) is prompted to review its etiology and pathogenesis up to the present time. It seems now pretty well agreed that the infectious agent is a filtrable virus, entering probably by the nose or nasopharynx, not by the skin. This specific pathogenic agent becomes localized simultaneously in ectodermal structures—the skin and mucous membrane—and in the tissues of the sensory nervous system. It may travel from the cortex to the periphery or *vice versa*, vaccinating the neural structures along which it travels, which serve as its culture medium.

Theories of the pathogenesis of herpes zoster have entirely changed, it is no longer considered to be a ganglionitis alone, but rather an ascending or descending infective process due to a specific filtrable virus with definite serum reactions and antibody production. In the affected nerves, lesions ranging from inflammation to hemorrhage and actual necrosis are found not only in ganglionic struc-

tures, but also along the nerve sheaths to the periphery, and ascending even into the medullary nuclei; some report involvement of the cortical region concerned. Histologically, the external manifestations observed are lesions of ectodermal structures due to selective action of the virus on the peripheral sensory neuron.

*Predisposing factors* seem to include excessive heat or cold, exposure, severe physical trauma, nervous shock or exhaustion, and sudden loss of endocrine equilibrium. Granulomatous ailments such as tuberculosis and syphilis seem to increase the vulnerability of peripheral neurons to the specific toxin of this disease. It has been suggested that chronic septic states caused by long-standing colonic stasis, cholecystitis, dental apicitis or nasal sinusitis may similarly facilitate meningeal invasion by the herpetic virus.

*Pathology.*—The skin lesion of herpes zoster, a vesicle, resembles that of smallpox but contains more exudate; it is due to intercellular edema with local necrosis and the appearance of Unna's "balloon" cells, large, swollen and multinuclear. Late skin changes include a thickened stratum corneum and proliferation of pigment cells, with depressed fibrotic zones when secondary infection has occurred.

The peripheral nerves at first show lymphocytic infiltration and small hemorrhages in their interfibrillary spaces. So-called oxyphilic inclusions—"herpetic bodies"—are later found along the nerve sheaths. The sensory ganglions show both interstitial and periganglionic round cell infiltration and occasionally necrosis.

*Symptoms.*—Symptoms and signs, in addition to vesicle formation (which may be limited to the posterior wall of the external auditory meatus or to 1 or 2 small lesions on the concha or mastoid), include pain, which may rarely disappear on drying of the vesicles, but usually lasts weeks, occasionally months; an enlarged preauricular lymph node (occasionally mastoid, cervical or parotid); loss of local tactile sensibility; and sometimes vesicles on the anterior two-thirds of the tongue, the anterior pillar or soft palate of the same side. Facial paralysis may supervene 4 or 5 days after, rarely coincidental with or preceding the eruption. Extensiveness or depth of vesiculation has nothing to do with the advent of paralysis. Pain accompanying facial palsy should always suggest herpes zoster. Vestibular and auditory symptoms, *i. e.*, moderate vertigo, slight deafness or buzzing noises, may precede the eruption by several days or appear simultaneously. Transitory in character, the dizziness is usually more annoying than the hearing disturbances. Various combined nerve involvements have been reported; both facial and auditory nerves; one branch of the fifth; the first cervical, and, rarely, one intercostal nerve along with various cranial divisions.

*Differential Diagnosis.*—The differential diagnosis must be considered from the various angles of the symptoms which are present. The diffuse and painful swelling over the mastoid, concha and posterior wall of the external canal must be differentiated from *mastoiditis*, *tuberculosis*, *eczema* about the canal, *erysipelas*, *fungus* invasions of the meatal epithelium, and *myringitis bullosa*. In the absence of middle ear infection, facial paralysis accompanied by severe pain suggests certain remote possibilities, such as *basal skull fracture* with hemorrhage into the internal auditory meatus, *exposure*, *syphilis*, and *tumors* or *cysts of the cerebellopontile angle*.

Severe pain in the facial sensory distribution, relayed at the geniculate ganglion from the great superficial petrosal and vidian nerves, may be caused by *sinusitis* affecting the sphenoid or posterior ethmoid, and rarely by various *irritative or malignant lesions of the nasopharynx, larynx and basilar process*. Here, again, close observation will disclose no skin lesions and rarely any enlarged or painful glands, unless very severe sinusitis or a metastatic malignant condition is present. *Neuralgias* due to dental caries, use of arsenicals in root canals, impacted third molars, undescended cuspids, cysts, osseous tumors of the jaw and like conditions are similarly easy to segregate, if necessary by x-ray evidence, from the pains of herpes zoster. Disturbance of other nerves than the seventh and eighth is uncommon. Nevertheless in those cases of herpes zoster associated with marked meningeal symptoms (the so-called encephalitic type), numerous other nerves of either side may be involved, notably the maxillary and mandibular divisions of the fifth. Thus, palatal, nasal and labial herpes may accompany herpes zoster oticus, usually at the start, activated apparently by the same dose of virus in adjacent regions of the medulla. Disturbance of taste without facial palsy and, very rarely, slight involvement of the forehead from the ophthalmic fifth have been reported but are of brief duration.

Symptoms referable to the brain and meninges, *i e*, violent, boring or band-like headaches, often with transitory rises in temperature and mental irritability and confusion, may suggest analogies to other diseases of these structures. Such conditions include *intracranial hemorrhage* in *hypertension* or *thrombosis*, when blood-pressure is low, prodromal stages of *encephalitis* or of *epidemic cerebro-spinal meningitis* or by extension of *intracranial neoplasms or abscesses*.

**Treatment.**—The management of herpes zoster oticus, according to Fenton (*Ibid*), is symptomatic. So far, since the virus has not yet been isolated, no specific treatment is possible. The serum of cured cases has been stated to attenuate or shorten the duration of postherpetic pain. "Shock" treatment has been advocated, *i e* **foreign protein injection**, as well as **autohemotherapy**, from 5 to 10 c.c. of the patient's own blood being used intramuscularly. Recumbency aggravates the pain of herpes zoster, such individuals are better off out of bed, unless they have a fever or other complications. **Ultraviolet irradiation** is found very helpful in shortening the duration of the pain.

*Locally*, dry open treatment with **nonirritating powders** or **mild, quick-drying antiseptics** will obviate secondary infection of the vesicles and prevent scarring. **Cocainization of the sphenopalatine region** is often very helpful in cutting down pain and vertigo at the period of geniculate ganglion swelling. The middle ear should be left severely alone unless an intercurrent otitis media requires surgical measures, a very rare complication. After the congestive stage has passed, **diathermy** may be tried if residual pain is excessive. **Alcohol injection of the sphenopalatine ganglion** and **pericarotid sympathectomy** have been tried, but confirmation of their good effects is conspicuously lacking.

Since the facial paralysis usually clears up within a few weeks, faradic treatment or operative procedures for decompression of the seventh nerve should not be considered until the paralysis has lasted, unchanged, for at least 2 or 3 months. Every case of Bell's palsy should be closely examined for traces of herpetic

vesicles, and in case of doubt a complement fixation test against a known herpes zoster virus should be made.

**Protein therapy** in the treatment of *infectious acoustic neuritis* was used by P. Zaviska (Monatschr. f. Ohrenh. 68:25 (Jan.) 1934). He treated 26 patients with impaired hearing due to neuritis of infectious origin with injections of various foreign proteins. There was marked improvement in hearing in nearly all instances. Leukocytosis was found to follow the injections of protein in a few hours. However, the author feels that the favorable results obtained were due not only to the leukocytosis, but to some substance produced which weakened the action of the toxins or other bacterial poisons.

**LABYRINTHITIS.**—In presenting 2 cases of suppurative labyrinthitis, N. Bentley (J. Michigan M. Soc. 33:69 (Feb.) 1934) accepts the classification of the Vienna school, *viz.*, (1) circumscribed, (2) diffuse serous, (3) diffuse purulent manifest, and (4) diffuse purulent latent labyrinthitis. Both of his cases had a labyrinthectomy and made uneventful recoveries.

**Treatment.**—Perhaps the most comprehensive presentation of the year was devoted to the treatment of labyrinthitis by I. Friesner and H. Rosenwasser (Arch. Otolaryng. 20:139 (Aug.) 1934). They review the histologic bases for clinical concepts of diseases of the labyrinth and include a very extensive bibliography of the literature from 1684 to the present time. Despite the voluminous literature on this subject with its innumerable reports of cases, there still exists a wide difference of opinion with regard to the surgical therapy in some forms of labyrinthine disease. However, there is considerable accord as to the treatment of *circumscribed labyrinthitis*. The term circumscribed labyrinthitis is used to signify disease of the labyrinthine bony capsule without diffuse involvement of the endolabyrinthine structures. Nearly all agree that the treatment for this condition is careful and complete **radical mastoidectomy**. It is perhaps unwise to attempt skin grafting on such a radical cavity at the primary operation.

*Latent labyrinthitis* is a condition in which the labyrinth has been the seat of a diffuse inflammatory process which has resulted in the total loss of function and of irritability and from which there are no longer any so-called labyrinthine symptoms. In order to appreciate the significance of this condition, some consideration must be given to the pathologic changes which may occur in the endolabyrinthine spaces as sequences of such diffuse inflammation. (1) The labyrinthitis may heal, and still the endolabyrinthine spaces may be filled with fluid and communicate directly with the subarachnoid space. (2) The labyrinth may be the site of reparative processes, which may arouse a rapid formation of new bone, and the endolabyrinthine spaces may be partially or completely filled with this new bone. With regard to these *two forms* of latent labyrinthitis, Friesner and Rosenwasser feel it must be obvious that no dependence as to surgical indications can be placed on the loss of function and of irritability; nor is the compensation phenomenon of Ruttin an adequate criterion. Even following extreme cases of labyrinthine necrosis, they have seen a reproduction of the promontory, concave instead of convex, analogous to the reproduced mastoid cortex, as well as a bony closure of the oval window. In the second variety of latent labyrinthitis, reparative processes have taken place in the endolabyrinthine

spaces subsequent to the diffuse infection, and the labyrinth is filled more or less completely with new bone. There is a tendency for new bone to form rapidly within the infected labyrinth. The conclusion arrived at is that "it is obvious that a labyrinth so filled with bone must be innocuous, no longer the seat of an active infection and no longer requiring any surgical intervention."

The *third variety* of latent labyrinthitis does not differ from the first two so far as the loss of function and of irritability is concerned. In these cases, however, operation discloses a communication between the labyrinth and the infected middle ear, aditus or antrum. This may be apparent either through the presence of a fistula in the bony capsule or through changes particularly about the oval window. It may be evident that cholesteatoma has invaded the labyrinth. In this third type of latent labyrinthitis, what might be called normal reparative processes have not occurred, and even though there may be no symptoms, there still remains an active infectious process in the endolabyrinthine spaces. Such a labyrinth may be the seat of necrosis or even of sequestration. It should not be regarded in any other light than as an unusually situated diseased mastoid cell which must be exenterated.

When this form of labyrinthitis is associated with any signs or symptoms indicative of an extension to the intracranial contents, it seems advisable that, combined with the **labyrinthectomy**, a wide exposure of the dura of both the middle and the posterior fossæ, with a careful search for an extradural abscess, be made.

The authors reserve the consideration of *diffuse manifest labyrinthitis* to the last, because it is this type concerning which the widest differences of opinion still exist. It has been customary to divide acute manifest labyrinthitis into 2 groups: (1) serous and (2) suppurative. As a matter of fact, this grouping has resulted from an attempt to classify clinically identical phenomena on the basis of pathologic evidence. In other words, the clinical phenomena have been studied through a microscope. The authors believe we have fallen far short of the actual differentiation between these two states because the clinical criteria advanced have been inadequate to establish accurately such a differentiation. So-called serous labyrinthitis has been considered as a collateral edema or a "toxic reaction."

**Types of Labyrinthitis**—*Traumatic Labyrinthitides*—The variety of labyrinthitis which occurs consequent on the evulsion of the stapes during the performance of a radical operation on the mastoid is an extremely serious condition, frequently followed by an extension of infection to the meninges. Some believe that patients with this complication should be afforded whatever safeguard can be given them by an immediate **labyrinthectomy**, while others believe that equally good results are obtained by treating these patients **conservatively**. If alarming symptoms ensue, they perform a labyrinthectomy.

*Extensive Necrosis of Petrous Pyramid*—In case of extensive necrosis of the petrous pyramid when the removal of a sequestrum or necrosed bone entails the opening of the endolabyrinthine spaces, a **labyrinthectomy** offers a better chance than conservative waiting.



*Diffuse Manifest Labyrinthitis.*—In the type of diffuse manifest labyrinthitis that occurs late after an infection of the middle ear, particularly in the presence of a latent mastoiditis, the tendency toward limitation of the process to the labyrinth and healing is extremely small and the possibility of extension to the cranial contents menacing. This represents one of the most disastrous types of labyrinthine infection and requires not only **exenteration of the labyrinth** but also an **exposure and search of the dura of both the middle and the posterior fossæ**. There is no difference of opinion concerning the handling of these cases.

*Labyrinthitis with Acute Otitis Media.*—In the type of labyrinthitis that occurs with acute otitis media, particularly when the labyrinth is involved during the first few days of the otitis, a more conservative attitude may be taken. In this group should also be included cases of labyrinthitis that follow shortly after a myringotomy and are probably traumatic. Apparently the annular ligament of the oval window may be torn by dislocation of the stapes. Total deafness with loss of irritability may follow rapidly, and yet the endolabyrinthine spaces may be infected either mildly or not at all. In other words, it is quite conceivable that trauma alone may be the cause of a loss of labyrinthine function without serious infection of the interior of the labyrinth. Friesner and Rosenwasser (*loc. cit.*) believe that in this type of case nothing is lost through conservative treatment.

There is no evidence to the supposition that repeated lumbar puncture and cytologic study of the spinal fluid alone can give criteria that might be used as a definite index of the degree or rapidity of extension to the meninges and so furnish the operative indication for **labyrinthectomy**. The authors are inclined to use this diagnostic measure only when it is definitely indicated. Lund, who is a protagonist for the use of lumbar puncture and cell count as an indication for labyrinthectomy, made the following statement: "If one does not start with the fact that normal cerebrospinal fluid is free of cells and that consequently from 3 to 6 cells per cubic millimeter is without doubt of pathological significance, then studies of the cytology of the cerebrospinal fluid are without value as an indication for labyrinthectomy." It is the majority who believe that in labyrinthitis, as with other conditions, clinical phenomena are more valuable than laboratory data as indications for operation.

**LABYRINTHINE CONCUSSION.**—A complex of clinical symptoms, especially present in cranial trauma (unilateral or bilateral difficulty in hearing, deafness, ringing in the ears, vertigo and headache) is interpreted as *commotio labyrinthi* or labyrinthine concussion.

Professor Voss, of Frankfort-on-Main (J. A. M. A., Berlin Correspondent, 103-1721 (Dec. 1) 1934), who has been occupied with these questions, has suggested that a summary be made of all changes in the inner ear which appear as a result of trauma to the cranium or spinal column. There is the possibility of similar symptoms in injuries on a distant part of the body, as on the feet or on the buttocks, because the percussion wave is transmitted from them through the spinal column. A number of clinical observations of labyrinthine diseases in gunshot injuries of the cranium make it certain that both types of injuries must

depend on the same or similar physical phenomena. In the small "cerebral concussions," as in *commotio cerebri*, it is a question of a rise in pressure in the labyrinthine secretion, which, according to the laws of hydrodynamics, may be transmitted in the direction of the percussion or to all sides. Thus under certain circumstances, the labyrinthine capsule may explode, as has been proved by Voss in patients having sustained war injuries. In case of weaker impacts, it is assumed that the nerve constituents enclosed within the labyrinthine capsule may be damaged or destroyed. This theory was previously not accepted by otologists, even by Voss, on the ground that the organ of Corti, because of its double embedding in fluid, is ideally protected against lesser concussions. In estimating such cases, they should be treated as traumatic neuroses. Microscopic observations, though few, which have been recently discovered, point to an organic basis for labyrinthine concussions. It is a question of degenerative processes to the nerves and to the organ of Corti. In addition, such degenerations may develop not only through impact of the fluid, but also through hemorrhages, as Voss himself has observed. Labyrinthine concussions with simultaneous fracture of the labyrinthine capsule may likewise occur. Animal experimentation, undertaken by Voss, showed consistent hemorrhages, especially in the perilymphatic spaces of the cochlea and between the branches of the cochlear nerve, while the vestibular semicircular canal apparatus remained untouched.

Voss concludes that there is a concussion of the labyrinth in the sense described. Organic changes may be the basis for these labyrinthine concussions, at least of cases of more pronounced auditory disturbance or of deafness of unresponsiveness or of poor responsiveness of the vestibular apparatus.

**OTITIS MEDIA**—*Otitis Media and Diarrhea in Children*.—Clinical analysis of the acute diarrheas in more than 100 children by H. Brokman (Schweiz. Med. Wchnschr. 64: 208 (Mar. 10) 1934) showed that the principal symptoms were otitis media, diarrhea, disturbances in the intermediate metabolism and disturbances of the central nervous system. Pathologic, bacteriologic and serologic investigations corroborated the clinical unitarian theory. A number of disease entities, which so far were considered otogenous sepsis, atypical alimentary intoxication or atypical dysentery, have become a unit. The primary etiology is still unknown and the pathogenesis has been cleared only partly, but this point of view is an attempt to form a new clinical, therapeutic and epidemiologic foundation for these serious disturbances occurring in small children.

Mastoid infection and nutritional disturbances in infants was discussed by T. S. Burgess (Ann. Otol. Rhin. and Laryng. 43: 606 (June) 1934), who reported several cases. In none of the cases was surgery resorted to before the effect of the medical treatment could be determined. Every effort in this direction was made until it was established beyond a doubt that the child would not recover on this régime alone. There was no change in the pediatric management after operation, so that the striking improvement in each case could be positively attributed to the removal of the focus within the mastoid. Burgess feels that there is ample anatomic, pathologic and clinical evidence to substantiate the belief that infection within the mastoid may have a profound systemic effect in infants. Mastoiditis associated with a marked nutritional disturbance creates a vicious

circle depending upon the interplay of the forces of individual resistance and infection. Break the circle and the child will recover. Increase his resistance by medical therapy and he may conquer the infection; or relieve the mastoiditis by surgery and he will respond to dietary treatment. The classical signs of mastoiditis do not present themselves because the patient has not the resistance to develop sufficient local reaction. Consequently the indications for operation are mainly pediatric in nature. It is wise, Burgess states, not to operate during the initial abrupt loss of weight. Careful pediatric management will usually check this abrupt loss, when surgery may be more safely performed.

**Complications of Otitis Media.**—**BRAIN ABSCESS.**—An account of his experiences in otogenic brain abscess, comprising 56 cases, was reported by Y. Meurman (*Acta Oto-laryng.* 19. 387, 1934). In this group, which consisted of material gathered from 1901 until 1932 (26 of the cases were since 1926), there were 31 who had abscesses of the cerebrum (group I), 24 of the cerebellum (group II) and 1 had a combination of the two. Only 9 followed an acute suppurative otitis media, while 47 were the result of chronic suppuration.

**Symptoms.**—Regarding the symptoms, *papilledema* was found about equally in the two groups and a *slow pulse rate* was found oftener in group I. In comparing the two, the pulse rate was found to have a greater tendency to diminish in the group of cerebral than in the group of cerebellar abscesses, and that the *lumbar pressure* cannot be the sole determining factor in lowering the pulse rate. *Low temperature* was very characteristic. There was *nystagmus* in 30 per cent of the cerebral cases, but a spontaneous nystagmus is not necessarily a symptom of an affection in the posterior fossa. Meurman found that a considerable pleocytosis in the spinal fluid need not always be prognostically unfavorable.

The *causa mortis* in group I was meningitis in 50 per cent and a high intracranial pressure in 25 per cent, whereas, in group II it was almost the reverse, being 47 per cent in the latter and 27 per cent in the former. Meurman warns that spinal fluid must be withdrawn slowly and only a few cm are to be removed. These rules were not followed in two of his cases which died following spinal puncture.

**Complications**—It is a well-known fact that a tumor below the tentorium may cause *sudden death* when increased intracranial pressure is quickly released by spinal puncture. Such death is produced by pressure upon the respiratory centers in the medulla as it is forced into the foramen magnum. This complication of *cerebellar abscess* is so rare that G. B. Fred (*Laryngoscope* 44:550 (July) 1934) reports an autopsied case of respiratory paralysis with such findings of a herniation into foramen magnum. He advises that if respiratory difficulties are encountered in the course of a mastoid operation, pressure on the medulla should be considered and an emergency exploration for cerebellar abscess instituted.

**Treatment**—As to the **surgical treatment**, Meurman feels that cases of brain abscess should be treated by only the most experienced surgeons. In his clinic they have not made a separate trephine opening, but usually employ an **osteoplastic flap**, exposing better the temporo-sphenoidal lobe area. A heavy cannula attached to a syringe is used for dural puncture instead of a knife, which he feels

is rough and a dangerous procedure, and pus is not so likely to be obtained through a stab wound. The percentage of group I cases cured was 29 and in group II there was 29.2, better results being obtained in recent years.

K. W. MacKenzie (J Laryng and Otol 49:357 (June) 1934) reports 8 cases of brain abscess, 6 of which were cured. Seven of the cases were the result of chronic suppurative otitis media. Four of these were temporo-sphenoidal lobe abscesses, 2 of which were cured, and 3 were cerebellar abscesses, all of which were cured. In 6 of the 8 cases **drainage** was done at operation and all the patients recovered. A decompression operation was performed in one of the remaining 2 cases, but before a final operation for drainage of the abscess could be carried out the abscess burst into the ventricle and the patient died. In the other, an exploratory operation was undertaken without success, but ultimately the abscess burst through the surgical wound and the patient died 8 days later.

In the treatment of a furuncle or an abscess, incision before it is considered "ripe" delays healing, but if operative intervention is postponed until local immunity has developed and a wall of inflammatory tissue has surrounded the pus, evacuation of the contents is followed by rapid cure. Just as too early incision will delay healing, so also will unnecessary delay be injurious. It is the author's procedure to *postpone operation until pressure symptoms have become well marked*, by which time a local immunity has been developed. Besides this development of immunity, delay renders the discovery and drainage of the abscess easy and also results in an immediate hernia of the brain on incision of the dura, which, by compressing the dura against the bony margins of the trephine opening, lessens the risk of the onset of meningitis. In 7 cases drainage was done through a clean trephine wound of from 1 to 1½ inches in diameter, situated either in the squamous portion of the temporal or posterior to the sigmoid sinus. In the eighth case of frontal lobe abscess, drainage was effected through the opening caused by an osteomyelitis of the frontal bone.

The author concludes that a "delayed" operation is necessary for success and that drainage through a large trephine wound is more likely to be successful than through the mastoid alone. This allows the removal of the brain tissue sloughs, which, if retained, are liable to give rise to fresh abscess formation. The retention of tubes beyond 48 hours is unnecessary in most cases, for invariably by that time the hernia has forced them out, along with sloughs of brain tissue. In seeking for an abscess it is an advantage to use angular forceps, as the blades can be expanded and so allow the pus to escape.

The *leaking brain abscess* is also discussed by D. McKenzie (*Ibid*, 48:797 (Dec.) 1933), who reports the spontaneous rupture and gradual discharge of a brain abscess. He states that, while symptoms may be so mitigated by the leakage that the evolution of the disease is spun out, its progress continues to be downward and the end, though delayed, is seldom in doubt. Sooner or later the surgeon must intervene to improve drainage. The intervention will depend on the actual quantity of pus discharged and on the patient's general condition and particular symptoms. Relief to headache and pain, even when complete and lasting, is not sufficient to justify a relaxation of vigilance, for a brain abscess may progress painlessly to a fatal issue.

In choosing a site for **drainage**, it is not wise to ignore the selection by nature of a certain point for drainage. Leakage, wherever it occurs, leads to the formation of a sinus with more or less firm and resistant walls. There is an inflammatory zone shutting off the infected from the uninfected meningeal and brain tissues around the tract. Within the limits of this area the surgeon can make incisions and insert tubes without much risk of spreading the infection. The apparently out-of-the-way fistula may really represent the site of origin of the abscess, and the stalk may actually be situated at that spot. In any case, it would probably be wise to combine drainage through an outlying fistula with drainage through the apparent site of origin, whether it is the nasal sinus or the ear. Or the fistula might be selected to begin with and if it failed to give the necessary relief, the original site could then be tried. When leakage is taking place through some inaccessible region, a direct opening should be made into the abscess. In the operation itself, safety consists in keeping as much as possible within the confines of the inflammatory zone round the discharging sinus. If the surgeon can offer sufficient drainage to the abscess without too rashly encroaching on the adjoining meninges and brain, he has done all that can be expected.

**FACIAL PARALYSIS — Etiology.** — Mastoiditis with facial paralysis in a 9-months-old infant is discussed by G. C. Saunders (Northwest Med. 33:330 (Sept.) 1934). The paralysis followed 48 hours after the ear began to discharge (paracentesis). The side of the face was flaccid and the corner of the mouth sagged. An **antrotomy** was performed but the face showed no tendency for the recovery of the nerve. The course was very slow. The mother was instructed to **massage** the face twice daily and **galvanic stimulation** of the nerve was done once a week. It was not until after 6 or 8 weeks that a return to function was noted and almost 6 months later the child was discharged with complete recovery.

The recent investigations of D. Wolff (Ann. Otol., Rhin. and Laryng. 43:193 (Mar.) 1934) point out certain very significant anatomic and embryologic facts, and offer a more plausible explanation of the early trauma of the seventh nerve. She states that the exposed condition of the facial nerve, as it occurs in the late fetus and early infancy, is of phylogeneticontogenetic and of clinical importance. She finds that a dehiscence or "aperture" of the facial canal occurs more or less constantly in infants in the region posterior to the oval window. This she correlates with the point of entrance of the stapedial artery into the facial canal, as seen in lower mammals with a stapedial artery and in humans with a persistent stapedial artery.

These observations offer a logical explanation of how a facial paralysis takes place in otitis media in infants, and leads to the suggestion that in such cases surgery is indicated at an early date in order to prevent extension of the danger.

**Postdiphtheritic Facial Paralysis** — On the basis of observation on 330 cases, H. Seckel (Deutsche med. Wchnschr. 59:1918 (Dec. 29) 1933) was able to corroborate the frequent appearance and disappearance of the facial phenomenon in all forms, but particularly in the severest forms of diphtheria. The incidence was about like that reported by Borrino (16 per cent.). Unilateral facial paresis, however, is much more rare after the generally bilateral pharyngeal diphtheria. The author observed it only 4 times (once without preceding facial phenomenon).

in 330 cases (1.2 per cent), but this percentage is high in view of the fact that other authors observed not a single case in still larger materials, and another one only 15 in more than 6000 cases. Three of the cases of postdiphtheritic facial paresis with the facial phenomenon, which were observed by the author, are reported. In the first 2 cases the facial phenomenon was first negative, and in the third case it was positive on the third day. The severity of the phenomenon varied in the 3 cases from a slight twitching of the corner of the mouth to a twitching of the entire half of the face. The facial paresis was, of course, absent in all 3 cases during the first stage, and a complete facial paralysis did not develop in any of them. The mild form of facial paresis became manifest only in the course of emotional excitements (laughing, crying, etc.), but in the severe forms it could be perceived by a lay person even when the face was calm.

The author differentiates 3 stages in the course of postdiphtheric facial neuritis: (1) The *initial or irritative stage*, during which the facial phenomenon is positive on both sides. Pains may develop on the side that later develops a paresis. (2) The *preparcitic stage*, during which the facial phenomenon that during the first stage had become positive, becomes weakened or negative on the side that later becomes paretic. On the contralateral side, the Chvostek sign remains unchanged or increases. The first two stages last from 16 to 26 days. (3) The *paretic stage*. On the side on which the facial phenomenon has become weakened or negative the paresis develops. The Chvostek sign of this side occasionally is positive, irrespective of the paresis. The facial phenomenon of the other side may become weaker or entirely negative. This signifies a return to normality. If, after from 2 to 6 weeks, the facial paresis disappears, the Chvostek sign is negative on both sides.

**LATERAL SINUS INJURIES**—Accidental injury of the lateral (transverse) sinus during mastoidectomy was discussed by H. Dintenfuss (Arch. Otolaryng. 20: 595 (Oct.) 1934) who made an effort to study and correlate data concerning accidental injuries of the lateral sinus during mastoidectomy. Injury of the lateral sinus admittedly increases the risk of the operation.

When the mastoid is large and pneumatic, the space between the lateral sinus and the posterior wall of the canal is broad, injuries of the sinus are less apt to occur, therefore, than in the small sclerotic mastoid, where the space between these structures is narrow. Injuries to the sinus appear to be more frequent in the right mastoid in men and in the left mastoid in women. Absence of the sinus plate or adhesions of the sinus to surrounding structures predispose to injury. The employment of the curette in removal of bone is more likely to be accompanied by trauma to the lateral sinus than is the use of any other instrument. The use of the gouge is attended with least danger. It seems wise to avoid the use of curettes, especially the narrower ones, when removing bone in close proximity to the sinus.

Bone in the immediate vicinity of the sinus should be removed last in all operations on the mastoid, for if the sinus is traumatized, the danger of infection is less, all the diseased tissue with infecting bacteria having been removed. There is also the advantage that the operative procedure will not be interrupted by hemorrhage. The principal *complications* of injury to the sinus are hemor-

rhage, secondary rupture of the sinus, septic thrombophlebitis and air embolism. Infection following injury of the sinus is usually due to the virulence of the organism of the diseased tissues. Infrequent change of packing is another contributing factor. Thrombi in the lateral sinus following accidental injury may become organized and remain so, or they may disappear spontaneously by secondary absorption, the sinus regaining its patency.

The *treatment* of injury to the sinus consists primarily of arresting *hemorrhage* by placing **tampons** in the operative cavity, and then obliterating the lumen of the sinus by introducing gauze between the sinus and its bony covering above and below the site of injury. *Infections of the blood stream* should be controlled by **intravenous medication, blood transfusions and ligation of the jugular vein**. It is probable that the occurrence of *septic thrombophlebitis* following mastoidectomy is a sequel, in some instances, of accidental injury of the sinus not recognized at operation.

**LATERAL SINUS THROMBOSIS.**—*Pathology.*—Lateral sinus thrombosis, according to E. G. Gill (South. M. J. 27:718 (Aug.) 1934) is the most common of the intracranial complications following middle ear and mastoid infection. It occurs most frequently in men and in both acute and chronic ear infections.

Sinus thrombosis may arise from other sources than the mastoid cells, *viz.* (1) infection from the scalp through the mastoid vein, occipital diploic and posterior temporal diploic veins, and through the superior longitudinal and the cavernous sinus. (2) The bulb may become involved by direct extension from the middle ear or from the labyrinth through the internal auditory vein and the inferior petrosal sinus. There may also be seen a thrombosis from infections in the neck. While these avenues of infection exist and must be recognized, the majority of all cases of involvement of the lateral sinus results directly from an extension of the mastoid infection with necrosis of the surrounding bone. Usually a perisinus accumulation of pus forms with bacterial invasion of the vessel wall. It is possible in practically all cases of sigmoid involvement to find a necrotic fistula in the bone extending from the mastoid cells to the sinus. Blood stream infections from thrombophlebitis of the sigmoid may usually be classed as the result of delayed or neglected mastoid drainage. A generalized infection following a suppurative process in the middle ear and mastoid is so often associated with sinus thrombophlebitis that the terms otogenous pyemia and sinus thrombosis are frequently regarded as synonymous.

*Complications.*—A *bilateral acute mastoiditis* with *lateral sinus phlebitis* complicating the course of an ethmoidal carcinoma was reported by R. P. Wright and J. W. Gerrie (Canad. M. A. J. 30:535 (May) 1934). Their patient, a woman of 63, was first admitted to the hospital in 1927, with a fungating mass protruding from the left nostril and extending to the inner canthus of the eye. Biopsy showed epidermoid carcinoma of low-grade cellular activity. Deep x-ray treatment was given, followed by interstitial and surface radium, the result being regression of the growth. Further courses of deep x-rays were given. In December, 1932, the patient was brought to the hospital by ambulance. Nine days previously, the fourth of a series of x-ray treatments had been given. Next day an acute bilateral otitis media set in, with perforation of both drumheads.

the external swelling increased, became red, and closed the left eye, and there were increasing deafness and stupor. As the symptoms became more severe, the left mastoid and lateral sinus were exposed. The mastoid cells and antrum were essentially normal, there being no free pus or breaking, and the lateral sinus did not appear sufficiently abnormal to warrant opening it. As the symptoms continued, 5 days after the mastoidectomy, the left jugular vein was ligated and the sinus collapsed. There was a dramatic fall in temperature, with amelioration of all symptoms and progressive, uneventful recovery. The authors leave open the question whether the septicemia was due to absorption from the infected carcinoma *via* the ethmoidal veins and cavernous sinuses, or from the mastoids *via* the lateral sinuses.

L. E. Wible and H. B. Slotkin (*Laryngoscope* 44: 736 (Sept.) 1934) present a case, in a child of 6 years, that illustrates the problem of a masked sinus thrombosis in the presence of a complicating *pneumonitis*. When surgical intervention was finally resorted to, the true state of affairs was disclosed only when an aspirating needle in the lateral sinus drew forth pus. Thrombosis was present despite the fact that the tunica adventitia presented a normal appearance. They stress an early diagnosis as being of paramount importance. The Tobey-Ayer test was of no value in this case and, according to the writers, may be misleading. Headache was not complained of. Papilledema, which was present, is seen more frequently with sinus thrombophlebitis than with either cerebellar or temporo-sphenoidal lobe abscesses. Metastatic arthritis were present and were represented by a subcutaneous abscess of the ankle and, later, by an arthritis of the sternoclavicular joint. In their experience, the sternoclavicular joint is the one that is involved most frequently with lateral sinus thrombophlebitis. It rarely suppurates and has been referred to as a toxic arthritis.

Two cases of *suppurative labyrinthitis* and sinus thrombosis are described by J. G. Druss (*Arch. Otolaryng.* 19: 671 (June) 1934). When these two complications coexist, they may be independent of one another or may be the cause of each other. In the latter event, the sinus thrombosis is usually secondary to the labyrinthitis by way of: (1) the preformed pathways (ductus and saccus endolymphaticus and labyrinthine veins), and (2) newly-formed pathways (erosion of bony capsule). Even histological study may not aid in determining the exact pathways from the labyrinth to the intracranial structures.

*Diagnosis*.—In the presence of a known mastoid infection before or after operation, if there is a sudden rise in temperature once or twice in 24 hours, with or without chills, it is an indication of a spread of the infection toward the blood stream. It is, of course, assumed that all other possible foci responsible for such symptoms have been eliminated. There is a pyemic, a septic and a septicopyemic form, of course, which may occur.

*Test for Thrombosis of Lateral Sinus*.—W. E. Dandy (*Ibid.* 19: 297 (Mar.) 1934) proposes a *ventricular hydrodynamic test* by which diagnosis of thrombosis of the lateral sinus may be made with the same degree of accuracy as that obtained with the spinal Tobey-Ayer test. Unilateral jugular compression (each side is tested separately) will cause the pressure of ventricular fluid to rise (with exceptions) if the lateral sinus is patent, and the level of the fluid will promptly



fall when the venous compression is released. If a rise of the ventricular pressure does not follow jugular compression on one side but follows compression on the other, the lateral sinus is probably occluded or absent on the former side. The use of this procedure instead of the spinal test is suggested only when a ventricular puncture is required to diagnose or eliminate the possibility of a tumor or an abscess of the brain by ventriculography. Under such circumstances it merely makes an additional spinal puncture unnecessary.

In cases where it is necessary to have a clearer picture of the possible presence of a thrombosis, P. Frenckner (*Acta oto-laryng.* 20: 477, 1934) suggests a method of *venosinography*. After the course of the longitudinal sinus has been marked off by a test x-ray exposure, with an indicator immediately above the occipital protuberance and another somewhat below the parietal protuberance, a 1-cm. opening is trephined between these two points just over the middle of the sinus. About 10 cc. of an opaque substance, "thorotrast," is injected while the patient is on the x-ray table. The results claimed are excellent, but the method has the great disadvantage of being an operative procedure and not without danger.

C. A. Froding (*loc. cit* 19: 338, 1934) in 14 cases was able to prove that a normal increase in the pressure in response to the *Queckenstedt test* by no means excludes the possibility of an obstructing thrombus being present. Of these cases, 11 had definite obliterating thrombi and 3 were tested after jugular ligation. This proves that this type of test is not as significant as it has hitherto been considered. The site of the thrombus and, perhaps, above all, its age certainly play an important part, since venous collaterals may develop in older thrombi. Even normally there are, in addition to the transverse sinus, other large blood passages from the cranial cavity. The cavernous sinus, for instance, is connected by way of the basilar sinus with the vertebral plexus. Another pathway of interest is the connection of the cavernous sinus with the inferior ophthalmic vein, which in turn connects with the pterygoid plexus. The latter empties by way of the anterior and posterior facial veins and the common facial vein into the internal jugular vein. This matter of communication certainly explains the normal rise in pressure in response to compression of the jugular vein in the neck, even when this vessel is thrombosed higher up. The same explanation will serve also for the cases in which the increase in pressure was normal after ligation of the vein, since such ligation is always applied above the area at which the vein empties into the common facial vein.

*Treatment*—The treatment may be divided into medical and surgical with equal emphasis. Good results have been reported from nonsurgical treatments, but the method of choice is to make intelligent use of both medical and surgical treatment. The most effective medical therapy is the **transfusion** of whole blood. This should be given while waiting for definite diagnostic symptoms, sometimes during the operation and during the period of convalescence. The hemoglobin concentration, the red blood count and the general well-being of the patient are the indications for the time to give the blood transfusions. If the hemoglobin content is 60 or below, Gill (*loc. cit*) gives transfusions every 48 hours. He gives from 100 to 150 cc. The importance of giving whole blood

at frequent intervals cannot be too strongly emphasized. A serious condition is being dealt with and a delay of a few hours, not days, often is the difference between success and failure. The donor and recipient should be carefully matched before each transfusion. Both may change. The use of **antistreptococcus serum** and **mercurochrome** have not been of value in Gill's cases. **Neoarsphenamine**, however, has been of definite value in all cases, small doses being given intravenously not more than once a week. Intravenous **saline** and **glucose** is often used with excellent results.

In regard to the **surgical therapy** Gill (*loc cit.*) feels that certain questions must be answered, *viz.*

1 In cases where thrombosis of the sigmoid sinus is complete, should the jugular vein be ligated?

2 Where there is complete thrombosis of the sinus, should all of the clot be removed in order to secure free bleeding?

3 What surgical procedure should be used in dealing with the vein (a) ligation, (b) ligation and division, or (c) ligation and resection?

4. What should be done with the facial vein?

5 What should be done with the external jugular and emissary veins?

6 Do the vein and sinus function after ligation?

It seems that the logical answers come from a consideration such as R. Almour proposes (*Laryngoscope* 44:454 (June) 1934) in a discussion of the basis for the selection of the type of procedure in sinus thrombosis. He emphasizes that the basic principles of such therapy are the essential anatomy, pathology and clinical experience. No doubt the three groups, those who ligate in all cases, those who ligate in selected cases and, lastly, those who contend that ligation is absolutely unnecessary, could profitably consider the facts and principles thus brought out by Almour, who recognizes that the results seem to differ in the various reports and that pros and cons are too conflicting to be properly evaluated.

The general conduct of the surgical side was presented by Froding (*loc cit.*) In acute otitis with clinical symptoms of thrombosis, mastoidectomy was performed and the sinus laid bare. If the wall of the sinus looked entirely normal, no operation on the sinus was performed, and expectant treatment instituted. If additional clinical symptoms of thrombosis then appeared, or if the sinus wall at the first operation looked suspicious, an incision was made in it. When this was followed by only very slight bleeding or none at all, the jugular vein was ligated, and the sinus bared further to the second bend and back until at least a few centimeters of the wall were free. Tampons were applied and the wall separated downwards and backwards until there was no doubt at all that the end of the thrombus had been reached. Gangrenous and decomposing sinus walls were extirpated, but complete thrombectomy was not done. In Froding's clinic no operations were performed on the bulb in the past 6 years. In chronic otitis, a radical operation is carried out and the sinus treated on the same principles as in the acute cases. In 56 cases the sinus was opened and the internal jugular ligated. In 2 cases it was opened and no ligation performed and in 3, only a mastoidectomy was carried out. He reports 17 deaths, a 72.1 per cent

of recoveries; 14 were in ligated cases, 1 in the opening without ligation, and 2 in the mastoid operation alone.

In brief, the surgical treatment consists of **elimination of the primary focus of infection, prevention of dissemination of the infection** from areas with thrombophlebitis, **drainage of the vein involved** and the **treatment of any metastasis**. The first step calls for a thorough **mastoid operation** simple or radical, depending upon the indications. Since it is not always possible to differentiate by symptoms and laboratory tests a sinus clot from bacteremia, the performance of a mastoid operation and free exposure of the sigmoid sinus is justified. Slightly more than the width should be exposed for inspection and compression if it is decided upon later. The appearance of the bony sinus plate is not to be relied upon. Ofttimes a sinus is found thrombosed or abscessed, yet the bony plate is apparently sound. The mastoid emissary should be exposed if present. If there is only slight evidence of phlebitis present, no other surgery is done. The wound is left open and particular care should be used in packing the wound. There is little likelihood that the sinus will become infected if the packing is not placed against it. If the septic symptoms are more pronounced and there is definite evidence of thrombosis, the **jugular** should be **ligated** and the **lateral sinus opened and drained**.

**OTOGENOUS MENINGITIS**—W. L. Gatewood and N. Settel (Arch. Otolaryng 18:614 (Nov.) 1933) describe a case of fulminant meningitis in which the primary otitis media had regressed and was apparently well on the way to resolution when, with a sudden onset, signs of fulminating meningitis appeared, with recurrence of the pain in the ear and development of the characteristic stiffness in the back of the neck. The patient died within 24 hours. The markedly increased pressure of the cerebrospinal fluid, together with the opacity and the greatly increased cell count of the fluid, could mean only well-established meningitis. When to this is added the presence in large numbers of streptococcus viridans in the fluid, there is additional evidence of generalized septic leptomeningitis. From their observations, the authors conclude that various pathways exist by which infection may pass from the middle ear to the brain. Extension by way of the blood-vessels or lymph canals leads rapidly to a diffused meningitis. Positive blood cultures are indicative of a hematogenous infection of the brain. The observations of the writers in their case pointed to the blood stream as the route by which the meninges were infected.

**Pathology**—The pathology and therapy of otogenic meningitis were ably considered by H. Neumann, of Vienna, (Acta Oto-laryng 20:102, 1934) who begins with the premise that it is unfair to count the number of cases of meningitis, but rather all of the factors must be carefully weighed. Meningitis is, as far as the histological studies show, an involvement of the dura, brain and choroid plexus. Its pathological anatomical changes are not alone local but also are concerned with changes in the liquor (spinal fluid) and general symptoms, which vary greatly in extent and intensity. The clinical symptoms are dependent upon local injury to the brain substance, the areas of the nerve foramina which are involved, the toxic destruction which has taken place and, lastly, upon the pressure conditions within the cranial cavity. The changes

in the spinal fluid consist of increased pressure, increased cellular elements, the presence of microorganisms and in abnormal physical and chemical constituents. Neumann presents a series of 59 personally studied cases of meningitis which occurred at the end of an acute otitis media. These were pure meningitis without other types of complications because actually his clinic had a combined material of 127 meningitis cases. The 59 cases which serve this particular study were divided into 2 groups: in Group I 38 cases (1928-1930) in which 23 died (61 per cent.) and 15 (39 per cent.) were cured; in Group II there were 21 cases (1931-1933), 14 (67 per cent.) died and 7 (33 per cent.) were healed; this makes a total of 37 (63 per cent.) cases of meningitis which died and 22 (37 per cent.) which recovered, 21 of these being under 15 years of age.

*Symptoms*—The cardinal symptoms of temperature, headaches, vomiting, Kernig sign, stiff neck, bulb, restlessness, irrational, hyperesthesia, dermatographia, Babinski sign, fundus changes and eye muscle paralyses, were compared in the cases which died and in those that survived. Invariably they were more often present in those who succumbed, especially was this true in regard to the Babinski test. The spinal fluids were next compared.

*Prognosis*—From his observations, Neumann believes that he is in a position to prognosticate definitely a certain group, *i. e.*, the cases of meningitis occurring in young individuals at the end of an acute otitis media, when a number of clinical symptoms are present, but weakly so. When it comes to the analysis of the cases which recovered, they are for the most part cases which were of a benign character, where it was due more to the nature of the process than to the manner of handling the case, although Neumann feels that the proper time of interference is of importance. He warns against waiting for full-blown symptoms of meningitis and particularly so in children who he found complained of generalized but not localized headaches. All his cases had a high temperature ( $39^{\circ}$  to  $40^{\circ}$  C— $102^{\circ}$  to  $103.5^{\circ}$  F) and on this basis alone feels that a diagnostic lumbar puncture is in order. In this same connection, the fact that the greatest number of recoveries were experienced in the young was explained by Neumann on the basis of the fact that spinal fluid changes manifested themselves earlier in the young and, therefore, meningitis was more promptly recognized, even before there was any thought of a meningitis. Thus is interference possible promptly when the opportunity for recovery is best. Prophylactically, only the most thorough mastoid operation, cleaning out every cellular group, is important. The earlier the operative interference, the better are the results which can be expected.

**OTOSCLEROSIS.—Pathogenesis.**—According to A. A. Gray (J. Laryng and Otol. 49:629 (Oct.) 1934), the essential causative factor of otosclerosis is a gradually increasing defect in the vasomotor mechanism which governs the nutrition of the structures of the organ of hearing as a whole. The axon reflexes are, of course, included in this vasomotor mechanism, and the stimulus which excites the vasomotor mechanism is sound and sound alone. Consequently, the vestibular apparatus and the semicircular canals are unaffected. There is no evidence whatever of any defect in any of the endocrine glands or their secre-

tions in otosclerosis. Neither is there any evidence of any defect in the bone metabolism of the body. On the contrary, the subjects of otosclerosis are, apart from their deafness, perfectly normal persons with ordinary average health. The deafness of otosclerosis bears little relationship to the extent of the disease in the bone. The deafness may be severe when the stapes is hardly fixed at all. The severity of the tinnitus bears no relationship at all to the extent of the disease in the bone. The extent of the change in the bone bears little relationship to the duration of the disease, but appears to depend on the age of the onset of the disease. The earlier the time at which the otosclerosis begins, the more extensive will the bone lesion become.

The deafness of otosclerosis is to a large extent functional and is the result of the insufficient supply of blood to all the nerve structures concerned in the perception of sound. The preponderance of women as subjects of otosclerosis is the result of the greater instability of their vasomotor system and the more frequent disturbances to which it is exposed. The changes in the bone show a remarkable bilateral symmetry, even to minute details. This symmetrical distribution is explained readily by the author's view of the causative factor of otosclerosis. The vasomotor nerves governing the nutrition of the organ of hearing are anatomically symmetrical like other nerve structures in the body. If, therefore, structural changes occur as a result of defective functioning of those nerves, such structural changes will be naturally bilaterally symmetrical in their distribution.

The pathogenesis of otosclerosis was divided into 2 main thoughts by F. Leiri of Helsingfors (*Acta Oto-laryng.* 19:427, 1934). His consideration was (1) concerned with the mechanical factors in the pathogenesis and (2) as to whether an electrochemical factor exists in the causation of otosclerosis

**PETROSITIS.**—A hitherto unknown entity has sprung into prominence by the association with an involvement of the petrous tip, a definitely demonstrable symptom-complex. During the past year there have been numerous contributions, all of which serve to firmly establish the identity of this disease. The literature, in the main, contains work of an anatomical nature which serves to make more certain the pathogenesis and the therapy.

The petrosal pyramid may consist of either pneumatic or diploic cells, either type of which may be recognized on x-ray films. True petrositis must occur in the pneumatic type, producing a coalescent infection with diminished aeration and increased density, resulting from subsequent osteitis. In a study of the temporal bones in a series of 100 autopsies, M. C. Myerson, H. Rubin and J. G. Gilbert (*Arch. Otolaryng.* 20:195 (Aug.) 1934) found pneumatization of the petrous apex in 11 per cent of the specimens. The ages of the patients varied from 7 months of fetal life to 89 years, but the pneumatization was not as frequent in children, as a matter of fact, it was entirely absent up to 7½ years of age. While invariably the apices were the same on both sides, the cellular structure of the mastoid portion and the petrous portion may differ. They found the best developed groups of cells around the jugular bulb and those above the cochlea. These findings were somewhat similar to those of E. W. Hagens (*Ibid.* 19:556 (May) 1934), who also found considerable variance in the

pneumatic process, although he found approximately 34 per cent. of bones studied had shown pneumatic spaces in the petrous tip. His measurements of the distance between the cochlea and the internal carotid artery just below the tegmen tympani likewise revealed a variability.

From a clinico-anatomical study, S L Ruskin (Ann Otol, Rhin, and Laryng. 42:961 (Dec.) 1933) concludes (1) that the venous pathways of the temporal bone play a leading rôle in the dissemination of infection from the tympanic cavity and the causation of intracranial complications; (2) that early extension of involvement of the venous system may be recognized clinically and should serve as a guide for early accurate intervention. Ruskin believes that the Gradenigo syndrome should be considered as venous engorgement symptoms and that the syndrome of temporomaxillary orbital pain, trismus and edema of the lower lid which he describes is of similar significance to the other syndrome; in the former, the group of tympanic veins empty into the inferior petrosal sinus, whereas, in the latter they drain anteriorly into the pterygoid plexus and middle meningeal vein.

Inasmuch as the distribution and extent of the cellular system of the temporal bone varies so, G E Tremble (Arch Otolaryng 19 172 (Feb) 1934) believes that the bone must be considered as a whole and not merely as a mastoid process. The numerous cellular areas are described. Connecting cells were found spreading forward from the antrum along the roof of the tympanum, above the superior semicircular canal, the cochlea and the internal auditory meatus, to reach the group of cells under the tegmen on the superior surface of the petrous tip. He, therefore, assumed that the probable pathway of an infection in the mastoid involving the tip of the petrous bone and causing paralysis of the abducens nerve takes place by one or the other of these routes.

In his yearly review of the problems concerned with suppuration of the petrosal pyramid, S J Kopetzky (*Ibid* 20 396 (Sept) 1934) comments on the confusion between Gradenigo syndrome *per se* and the true petrosal suppuration. He feels that those cases described under the Gradenigo heading do not show involvement of the petrous pyramid and cites Ruskin's case as an example of such a misinterpretation. It is Kopetzky's contention that the abducens paralysis results from meningeal involvement, which occurs late in the course of petrosal suppuration, as revealed by postmortem examinations. The sign, however, must not be construed as pathognomonic and petrous involvement may occur with or without abducens paralysis. He definitely disagrees with Ruskin's attempt to connect up the venous circulation with the syndrome or the addition of another symptom, *i e*, swelling of the lower lid, Kopetzky never having observed the sign in 31 authenticated cases of true petrosal suppuration.

From the foregoing it is seen that confusion has been prevalent surrounding the symptoms of so-called *Gradenigo's syndrome*. As originally described, these symptoms did not indicate petrositis, which may be present without paralysis of the sixth nerve. All cases of true petrositis occur in the pneumatized temporal bone, and the more cellular the petrous pyramid, the more evident is the tendency to suppuration. In these cases the pyramid is developed by pneumatization, as is the mastoid process. It is true osteitis, not osteomyelitis, since there is no

medullary cavity in pneumatized bone. Most of these cases have cells extending out into the zygoma. The infections of the mastoid and the middle ear usually clear up, and then after a quiescent period, profuse otorrhea marks the beginning of the petrositis. The acute cases, if untreated, may lead to meningitis. The chronic cases lead to a chronic fistulous discharge without meningitis. Few, if any, of the patients recover without some form of surgical intervention. In many of them the condition is accompanied by pain in the eye, on the side of the lesion, especially at night, and they often exhibit a low grade fever. In addition, there may be drowsiness, vomiting and irregular nystagmus. The cochlear and vestibular functions are usually normal. At this stage of the condition an x-ray examination will show changes if compared with a previous picture of the more normal state. These symptoms may, if neglected, disappear during a quiescent period, during which, however, the profuse discharge persists, with the sudden development of generalized meningitis.

In a rather extensive discourse presented as a contribution to the knowledge of the genesis of certain symptoms of apicitis, A. A. Sjöberg (*Acta Oto-laryng.* 19:479, 1934) attempts to explain the anatomical basis of the chief symptoms of the Gradenigo syndrome. He presents the case histories of 4 patients, 3 of which had x-ray evidence of apical involvement before the advent of typical symptoms, which he calls cases of *abortive apicitis*. It is quite clear that this author works on the premise that an apicitis would sooner or later develop a Gradenigo syndrome, so that this, to his mind, forms one group of *latent apicitis* in contradistinction to another group which manifestly has trigeminal pain, abducens paresis and roentgenologically demonstrable changes in the apex. Sjöberg feels that in the light of the fact that the abducens receives fibers from the ophthalmic nerve as it enters the orbit, it is very probable that the initial eye pains in some cases of apicitis may be irritated from these sensory ophthalmic fibers of the abducens nerve. These pains are then produced by pressure or toxic influence on the abducens in the canal under the petrosphenoidal ligament and thus need not be dependent on an irritation of the ophthalmic trunk itself.

X-ray changes in the petrous portion of the temporal bone without clinical manifestations are reported by G. M. Coates, M. S. Ersner and D. Myers (*Arch. Otolaryng.* 20:615 (Nov.) 1934). Their studies would indicate that by routine studies more unsuspected cases of petrous involvement in pneumatized mastoid will be brought to light. They feel, from their experience, that the condition need not indicate surgical intervention *per se*, but by a thorough mastoid operation recovery may be expected. A series of 9 cases, which resulted favorably, is presented to illustrate that radical surgical procedures should have a more definite indication.

**Treatment.**—To aid in the uncapping of the petrous apex, M. C. Myerson, H. Rubin, and J. G. Gilbert (*Ibid.* 20:575 (Oct.) 1934) have devised gouges and curettes so angulated as to make the approach less difficult. This same group likewise propose an improved **operative technic** (*Arch. Otolaryng.* 19:699 (June) 1934) calculated to be more conservative than that of Kopetzky and Almour and also of Eagleton. The technic removes a large section of the squamous bone down to the zygoma anteriorly and the knee of the sigmoid sinus

posteriorly, approximately 4 cm in diameter. The tegmen mastoidea and tympani is then removed as far as the prominence of the superior semicircular canal. Elevation of the temporal bone is carried out along the anterior surface, hugging the superior border of the pyramid. They used this approach to the apex in 2 patients.

In discussing the conservative treatment of petrositis, S. D. Greenfield (*Ibid* 20 172 (Aug.) 1934) believes that, in view of the fact that the discharge in petrositis does not originate in the tympanum but comes through the latter from the cells situated in the petrous pyramid, the presence of a profusely discharging ear in a case of petrositis should be regarded as a most favorable therapeutic phenomenon. He raises the question as to whether or not this perforating channel through the tympanum, spontaneously created, may not in some instances be sufficient to accomplish a cure without operative intervention. If such is the case, it may be advisable to postpone operation in patients in whom the aural discharge is profuse and in whom invasion of the intracranial structures does not appear imminent. That *spontaneous cure* does take place is confirmed by the fact that the vast majority of patients with the so-called Gradenigo syndrome recover without operation. Etiologically, the two conditions are identical. Anatomically, they both represent involvement along certain groups of cells leading to the region of the apex of the petrous pyramid. Pathologically, however, petrositis represents a more advanced, a more widespread and a more prolonged process. It has a tendency to involve the deeper cellular structures rather than the superficial. It is reasonable, therefore, to expect that a similar termination may be effected in the cases of petrositis in which the aural discharge is profuse. In many instances, there is no reason why the drainage from this route may not be sufficient to cause spontaneous resolution. The author reports 2 cases of petrositis in which no operation was performed because of the profuse aural discharge. Both patients recovered.

**VERTIGO.** In his paper, W. Bram (*J Laryng and Otol* 49, 153 (Mar) 1934) discusses *aural vertigo* and its differentiation from vertigo due to lesions elsewhere. A subjective sense of rotation, either of the patient or of his surroundings, is the commonest form of aural vertigo, but it is by no means always present. Vertigo is defined as the sensation of a disordered orientation of the body in space. It is because it is the sensory expression of a disorder of function which can be produced in many ways, that difficulty in estimating the significance and diagnosing the source of vertigo arises.

The *pathogenesis* of aural vertigo is in some cases easy to understand, but there are a large group of individuals suffering from "Ménière's syndrome" in which the pathology remains obscure. It is suggested that there is a condition of the labyrinth equivalent to papilledema, and many forms of retinitis seen in the fundus oculi. The venous drainage of the labyrinth is even more intimately related to the intracranial venous circulation than is that of the eye. There is probably no feature which is absolutely pathognomonic of aural vertigo, but certain features which in many cases help in its recognition, are reviewed. Attention is drawn to the points by which vertigo due to lesions of the eighth nerve differ



from those due to a lesion of the pons and medulla, intracranial tumors, epilepsy and other conditions.

**Etiology.**—Thornval (*Acta Oto-laryng.* 20: 443, 1934) examined 55 patients with Ménière's syndrome, all suffering from severe periodic attacks and also exhibiting symptoms. Some patients had up to 70 tests performed and in no instance did he find any definite sign of increased caloric reaction on the diseased side. In answer to the possible question as to what accounts for the violent paroxysmal attacks he states that "Ménière attacks are brought on by a sudden, often almost explosively developing hyperfunction of the vestibular system on one side." For analogy he asks the consideration of a periodic neuralgia in a nerve such as the trigeminal, the slight decrease in function, shown in certain cases, may correspond to a mild anesthesia in the peripheral area supplied by the nerve.

H Just (*Ztschr. f. Hals-Nasen-u. Ohrenh.* 35: 171 (Feb 10) 1934) believes that Ménière's symptom complex is nothing more than an angioneurosis especially of the acoustic nerve. He states that he has never seen active or latent Ménière's disease without unilateral or bilateral infection in the upper air passages and that the symptoms promptly disappear when the nasal condition is cured. Acute or chronic catarrh in the upper air passages, especially the sphenothmoid recess, and catarrh or purulent infection of the sphenoid sinuses or ethmoid cells are the most common etiologic factors. Decrease in acuity or hearing and a constant sensation of noise indicate permanent damage in the region of the nucleus of the cochlear nerve. Relapses after treatment of the underlying nasal conditions do occur. It stands to reason that new infections of the mucosa of the upper air passages in the course of influenza or other catarrhal infections may bring on a new attack of Ménière's syndrome. On prophylactic grounds, Just feels that persons disposed to catarrh should be given small amounts of iodide.

**Symptoms.**—The signs and symptoms and treatment of 42 cases of Ménière's disease were analyzed by W. E. Dandy (*Arch. Otolaryng.* 20: 1 (July) 1934). The disease was found to be twice as frequent in males as in females and more often on the left than on the right. The symptom of onset may be recurring dizziness, unilateral partial deafness or tinnitus in the affected ear, in about equal percentages. Nausea and vomiting were present during the attacks in all except three cases. At first the attacks usually occurred at infrequent intervals increasing in frequency, intensity or both. In most instances they occurred once or twice a month. The average duration of the attack was from 3 to 4 hours. The attacks might last for only a few minutes but frequently persisted for hours and even days. In most cases there was no recognized stimulus to bring on the attack, coming on usually without warning and developing with extreme suddenness. The character of the dizziness was most variable, always with a sensation of objects moving in a rotating fashion. Dandy found the direction of rotation valueless in determining the ear relationship to the nerve involved. It would have been an invaluable guide in determining the side of the lesion in cases of Ménière's disease and pseudo-Ménière's disease (Dandy believes they are the same) before the onset of deafness. He found deafness in some degree of a unilateral character in every case but not of a special type nor did he feel that

the caloric test was of much value in determining the degree of vestibular function. His cases showed miscellaneous other signs and symptoms which could not be considered diagnostic.

**Diagnosis.**—Dandy (*Ibid.*) finds the diagnosis of Ménière's disease rarely difficult with the triad of deafness, dizziness and tinnitus present. In pseudo-Ménière's disease only the dizziness is present.

As the result of experimentation over a period of years, A. Thornval (*loc cit.*) believes that he has a practical *caloric test* to demonstrate the reaction in morbus Ménière. "The principal of the method consists of first measuring the patient's rectal temperature and then as far as possible his caloric reaction in 2 positions, ventral and dorsal decubitus. These two positions are used in order to get uniform experimental conditions so that there is a vertical line from the external canthus to the uppermost border of the external meatus" A thermometer is built into the irrigating apparatus to measure the water as it flows into the auditory passage. The method is based upon the time it takes before the first nystagmus is observed, the duration of the nystagmus, and amount of water used. The observations are made with Bartel's electrical glasses.

**Treatment.**—In the medical treatment of aural vertigo, Brain (*loc cit*) has found **luminal** to be the most satisfactory drug. Small doses will often make a patient comfortable and larger doses may be given, if necessary, subcutaneously, during a severe attack.

J. Dundas-Grant (*Lancet*, 2, 1029 (Nov 4) 1933) is convinced that in suitable cases **ossicectomy** is of the utmost value. It does not do away with the necessity for the radical mastoid operation, but in certain cases presenting symptoms indicating radical procedure the operation of ossicectomy has relieved these symptoms and shown the radical operation to have been avoidable. Ossicectomy should be considered before such operations as obliteration of the labyrinth or section of the eighth nerve on account of vertigo are undertaken. Often the practiced eye will detect changes attributable to retractions of the membrane or fixation of parts produced by the residue of inflammation in the middle ear. In some of the 12 cases that the author describes the ossicles obstructed the outlet of the attic and prevented the escape of thickened discharges of cholesteatomatous collections and in others their fixation led to immobility of an otherwise mobile stapes. In the former the removal of the ossicles permitted the free escape of contents of the attic, with relief from vertigo and headache and, to some extent, from dullness of hearing. In the latter the restored mobility of the stapes provided the normal safety valve for variations of intralabyrinthine tension, with a disappearance of the distressing vertigo. He concludes that, in the normal subject, such removal would probably reduce the hearing to about 6 feet for the soft whisper, a useful but a much diminished amount of hearing power. In a patient having a greater degree of hearing, ossicectomy would, therefore, be undesirable unless called for by a major disability, the removal of which rendered a moderate reduction of hearing a matter of relatively minor importance. In most of the cases in which ossicectomy is required, the hearing power is less than this and the operation, while

making it no worse, sometimes makes it better than before, as in one of the author's cases.

In discussing the treatment of so-called *pseudo-Ménière's disease*, W. E. Dandy (Bull. Johns Hopkins Hosp. 55:232 (Sept.) 1934) differentiates between the classical syndrome of Ménière's disease and so-called pseudo-Ménière's disease by the hearing tests. In the former there is always unilateral subtotal loss of hearing, while in pseudo-Ménière's disease the attacks of dizziness and the character of the dizziness are precisely similar, but there is no unilateral symptom or objective change in hearing by which the dizziness can be localized to one side. He feels that the site of the lesion that is causing Ménière's disease is in the auditory nerve and not in the end organ. Since he treats Ménière's disease by sectioning the auditory nerve on the side known to be affected, it is very important to differentiate between the true and the pseudo-Ménière's disease, for in the latter there is no way of telling which side is the one involved. The substitution of hemisection of the auditory nerve in Ménière's disease, *i. e.*, total section of the vestibular branch with preservation of the auditory branch and its function of hearing, offers a solution to the problem of treating pseudo-Ménière's disease (this Dandy did in 3 cases). He also states that a large part of the cochlear branch of the nerve (nine-tenths in one case and more in another) can be sectioned without any appreciable (to the patient) loss of hearing and he offers an additional margin of safety in proposing **section of both auditory nerves** as a rational treatment for the cure of so-called pseudo-Ménière's disease.

Case of a male, aged 44 years, structural steel worker, with history of constant dizziness and dizzy attacks of  $7\frac{1}{2}$  months' duration, which came on suddenly when patient had gone to bed after a day's work, feeling as well as usual. Upon turning quickly from the right to the left side, there immediately followed a severe attack of vertigo. Tension varied from  $138\frac{1}{100}$  to  $180\frac{1}{120}$ . Laboratory tests were negative. Audiometer test showed 3 per cent loss of hearing on the right and 9 per cent loss on the left. Caloric test with cold water gave similar responses on both sides. Since there was no marked loss of hearing on either side, and because tinnitus was not referred to either ear, and since there was no discomfort in the region of either ear, a diagnosis of pseudo-Ménière's disease was made. Patient was operated upon (cerebellar approach) and the anterior five-eighths of each auditory nerve was divided. From the time of operation until last recorded postoperative date 25 days later, patient was annoyed by the sensation that the position of his head and feet could not be accurately estimated and appeared to continue turning after movement. His gait was still uncertain. All dizziness and tinnitus was gone. The author summarizes as follows: That the vestibular nerves were totally severed by the operation is shown by (1) irrigation of ears with hot and cold water gave no nystagmus and produced no subjective dizziness, (2) whirling tests with head bent forward produced no signs or symptoms. The audiometer findings postoperatively showed the hearing to be practically unaffected.

Dandy discusses the various *postoperative sequelae*, such as facial nerve injury (2 cases), transient Bell's palsy (3 cases), diplopia (4 cases), transient nystagmus and vertigo (32 cases), postoperative tinnitus (disappeared in 20 cases, unchanged in 17, and diminished in 2 cases). The effects on hearing after subtotal section of the cochlear branch of the auditory nerve he found to be *nil*.

Case of a woman, aged 62. Ménière's disease,  $\frac{1}{8}$ - $\frac{1}{10}$  of nerve remained after sectioning and audiometer showed loss of high tones above 1024, but the hearing was otherwise about the same as it was before operation.

Case of a man, aged 48, in whom less than  $\frac{1}{8}$  of the cochlear nerve remained intact. There was no difference in the preoperative and postoperative audiometer curves. He states that a very large part of the auditory nerve may be sacrificed and normal, or nearly normal, hearing still be retained, also that experiments on the auditory nerve are, therefore, quite similar to those of the trigeminal and optic nerves, in both of which a large volume of the nerve may be sacrificed without loss of function.

**ESOPHAGUS, LARYNX, PERORAL ENDOSCOPY, AND LUNGS.—ESOPHAGUS, AFFECTIONS OF.—Classification.**—Lesions of the esophagus are classified by W. F. Manges (Pennsylvania M. J. 37:1000 (Sept.) 1934) as: *Congenital*: (1) Complete atresia; (2) shortening; (3) fistula (tracheoesophageal). *Acquired*: (1) Diverticulum; (2) phrenospasm; (3) ulcer; (4) stricture; (5) foreign body; (6) newgrowth.

**CONGENITALLY SHORT ESOPHAGUS (THORACIC STOMACH).—Diagnosis.**—This must be differentiated from acquired stricture, peptic ulcer of the esophagus and diaphragmatic hernias of the stomach. L. H. Clerf and W. F. Manges (J. A. M. A. 102:2008 (June 16) 1934; Ann. Otol., Rhin. and Laryng. 42:1058 (Dec.) 1933) divide the symptoms into 2 groups, *i. e.*, (1) outstanding symptoms of dysphagia and regurgitation, with disturbances in nutrition and growth; (2) postprandial distress in addition to the symptoms of group (1). Dysphagia since birth, increasing with the addition of solid food, is significant in a history. Distress may vary from "indigestion" and flatulence to severe epigastric pain, occurring most commonly very shortly after taking food.

**Alkalis** give immediate relief, which is usually brief. Esophagoscopy examination in the latter types usually reveals ulceration. In these patients, Clerf and Manges produced the characteristic pain by swabbing the ulcer with silver nitrate solution and relieved it by preliminary topical cocaine. Microscopic study of tissue taken from above and from below the point of stenosis usually found in these cases will confirm diagnosis of thoracic stomach if stomach mucosa is found below and esophageal mucosa above. When the stenosis is of such caliber as to prevent passage of barium or the esophagoscope, no opinion can be given regarding the presence or absence of a congenital anomaly. A congenitally short esophagus with a peptic esophageal ulcer is reported by I. L. Haroen and P. G. Gerlings (Acta oto-laryng. 19:461, 1934).

**Treatment.**—Therapy is directed at providing an adequate food supply and the relief of pain, according to Clerf and Manges (*loc. cit.*). The first is to be sought for by dilatation, the second, by peptic ulcer régimes and topical applications of 10 per cent solution of silver nitrate.

**PHARYNGOESOPHAGEAL DIVERTICULA (PHARYNGEAL DIVERTICULA; LUDLOW (ZENKER) DIVERTICULA; PHARYNGEAL PULSION OR TRACTION DIVERTICULA).—Treatment.**—R. D. McClure (Am. J. Surg. 24:732 (June) 1934) attempts to present a modification of the various operative procedures available. The following was apparently devised in 1922 (date of operation reported) by the late Wendell T. Garretson.

A stomach tube was passed through the esophagus; another, No. 32 soft rubber catheter, was passed into the diverticulum and transfixed after the usual dissection, to the tube by one

plain catgut stitch. The diverticulum was then drawn into the esophagus and a purse-string silk suture placed at its base; further reinforcement was obtained by several fine silk sutures; one gauze drain was placed below and one rubber drain to the inversion site; usual closure. An attempt to pull the sac through and snare it off, using the Jackson pharyngoscope, was unsuccessful because of the size of the sac and its enclosed catheter. By the next day, edema of the mass caused such acute dyspnea that Garretson modified the original snare-program by removing the upper part of the sac which was attached to the catheter with a scissors. Next, with a tonsil snare, the sac was removed down at its base. Uneventful recovery followed, the patient was able to take and retain fluids on the fourth postoperative day. The drain had been removed by the first day and the wound subsequently healed by first intention. The patient died 8 years later, but with no recurrence of the symptoms of esophageal trouble.

McClure concludes that (1) the one-stage operation for the cure of pharyngeal diverticula is very successful in the hands of the most skilled surgeons; (2) the two-stage operation is the safest for the patient in the hands of the general surgeon and is a very generally accepted procedure today; (3) the inversion and snare operation is merely presented without any recommendations.

**ESOPHAGEAL VARIX.**—This is a rare occurrence in the young, being most often the result of such conditions as hepatic cirrhosis, Banti's disease and related conditions. E. Friedman (J. Pediat. 4: 641 (May) 1934) reports a case not dependent on liver cirrhosis, occurring in a 3½-year-old child. The bleeding began at the age of 18 months, did not recur for a period of about 1 year, and then began again for the third time 3 months later. Previously, recovery from hemorrhage usually took place in from 2 to 7 days. Fever accompanied each hemorrhage, reaching 104° F. (40° C.) The interim between hemorrhages was normal. Because of the severity of the hemorrhage, esophagoscopy was not performed. Finally, a massive hemorrhage resulted in death the second day after admission to the hospital. Postmortem examination revealed large venous plexuses of the esophagus, with occasional hemorrhagic areas in its lower aspect. The cardiac orifice of the stomach showed several small mucosal ulcerations. The spleen and liver were not enlarged.

**Ruptured Esophageal Varices.**—These varices are included in the group of hematemeses due to portal obstruction which comprises 5 per cent. of all cases of hematemesis, according to S. E. Russ (Texas State J. Med. 30: 250 (Aug.) 1934). Although he naively suggests prophylactic surgery in the nature of ligating the coronary gastric vein in cases of portal obstruction, he does not report having done this in his case that came to postmortem. General treatment is summarized as (1) **nothing by mouth**; (2) sufficient fluids by **hypodermoclysis**; (3) frequent small **transfusions of blood**; (4) **absolute rest** and relaxation obtained by **opiates**. Coagulants are of doubtful value.

**MOTOR DYSFUNCTIONS—Achalasia (Cardiospasm; Preventiculis).**—This condition is described by A. F. Hurst (J. A. M. A. 102: 582 (Feb. 24) 1934) in patients suffering from a hypochromic microcytic type of anemia; exceptionally it is Addisonian. Atrophic glossitis is constantly present. This condition of the mucous membrane extends to the pharynx and entrance into the esophagus. The associated dysphagia is a result of disturbance in the neuromuscular mechanism, which causes the relaxation of the normally closed pharyngoesophageal sphincter. Absence of this relaxation or "achalasia," is suf-

ficient to cause dysphagia, though in some cases spasm may replace the normal relaxation. Degenerative changes of the ganglion cells of Auerbach's plexus were found by Rake in 1927, so that Hurst's theory presented in 1913 concerning the neuromuscular character of this type of dysphagia was confirmed. General therapy is directed at the cause of the anemia when present. Local measures are best directed at the lower sphincter of the esophagus in the form of dilatation.

**FOREIGN BODIES.**—*Biplane Fluoroscopy.*—*Technic.*—The origin of biplane fluoroscopy is stated to have taken place in 1916 and is credited to G. W. Grier by W. F. Manges (Am J Roentgenol. 30: 674 (Nov.) 1933). Manges also states that the first report of the use of a magnet to influence the position of a metallic foreign body so that it could be successfully grasped was made by Hickey in 1910. Today, only by the use of biplane fluoroscopy is the removal of foreign bodies in the bronchioles and parenchyma of lung made possible. Other indications for its use are for the removal of opaque foreign bodies which are associated with a pathological process that interferes with bronchoscopic removal or which are associated with stricture of the esophagus. Removal of such bodies from the stomach is also enhanced by means of this procedure.

Manges warns against exposure of the head or hands of the patient, nurses, assistants, roentgenologist and endoscopist. To avoid such accidents, he exposes very small areas, divides the exposure as equally as possible in two planes, and at every possible opportunity turns off the current. Lights in the operating room are frequently turned on during such procedures to make certain that everyone is in a safe position away from direct exposure and points of electrical contact.

Also, an assistant keeps check on the time, calling out periods of time since the beginning of the operation. A period of 40 minutes is considered rather long, although Manges states that he has at times worked for even an hour. However, he interrupts the operation if he feels that the exposure has been great, unless some unusual emergency exists. Two weeks of rest are permitted to elapse before the second attempt is made. A few patients are reported to have had 2, 3, 4 or more such sessions before the foreign body was finally obtained.

Manges has shown in a simple but impressive manner that a certain philosophy is essential to any degree of success in the use of the biplane fluoroscope. First, terms that are used between the roentgenologist and the endoscopist should be of such character as to be clear cut yet terse, for example, "Go deeper," "Go forward," "Go back," "Go to right," "Open your forceps laterally," "Open anteroposteriorly," "Now close forceps," "Hold," "Without opening forceps go left, right, back, forward, deeper, withdraw slightly," "You have hold of the keeper," "You have hold of the spring," etc. Second, such terms do not alarm the patient who is usually awake. There is no doubt that it requires all the skill of a competent roentgenologist and competent endoscopist to cooperate with each other and train their assistants to do likewise in order to accomplish the feats of blind surgery, as far as the operator's eyes are concerned, that Manges reports for Jackson, Clerf and their associates.

**Unusual Sequence in Removal.**—Another case of interest is added to the literature of foreign bodies of the gustatory tract by P. P. Vinson and K.

Weissler (Am. J. Digest Dis. and Nutrition 1: 357 (Aug.) 1934) A child, 11 months of age, had swallowed an open safety-pin. During esophagoscopy, because of the low position of the pin with its open ends facing in the direction of the plane of removal and embarrassment of respiration, it was decided that it was best to push the pin into the stomach. Another x-ray examination made immediately showed that the pin had been regurgitated into the upper portion of the esophagus with its open ends reversed. The solution was thereby simplified, for the pin was then removed very easily by peroral endoscopy.

**Prophylactic Mediastinotomy.**—F. L. Lederer and L. Z. Fishman (Arch. Otolaryng. 19: 426 (Apr.) 1934) present an unusual case of multiple small and large sharp foreign bodies within the gastrointestinal tract. All of these were passed by rectum without complications. Case histories of esophageal foreign bodies from the literature and from their own experience are discussed, the outcome of which has shown that after a diagnosis of esophageal perforation has been made, there is no means available for determining in advance whether the conservative or radical form of intervention is indicated.

The problem particularly under discussion concerns the radical procedure of prophylactic treatment of lacerations of the esophagus. The method, termed "prophylactic mediastinotomy," consists of placing a drain into the prevertebral or pharyngobasilar fascia just below the site of esophageal laceration, immediately after the presence of such a laceration has been diagnosed. The purpose of this attack is directed at checking the future descent of an infectious process, should it take place, from the esophageal wound into the mediastinum. Instances of foreign bodies of the gastrointestinal tract which were apparently innocuous, yet resulted in serious complications, are discussed as being the antitheses of certain cases of perforating foreign bodies, balancing what Lederer and Fishman term, "the unknown equation." Prophylactic mediastinotomy is done frequently in Vienna and very infrequently in America. On the basis of the "unknown equation," the authors urge the use of prophylactic mediastinotomy conservatively.

Also, a case is described in which an open safety-pin was closed within the esophagus, using the Haslinger safety-pin closer. An attempt to withdraw the instrument and pin revealed that the pin had been closed onto the esophageal mucosa. Although the pin was removed only after enlarging the preexisting laceration of the mucosa, the patient made an uneventful recovery. Lederer and Fishman warn against the use of safety-pin closers. They offer valuable means of removing safety-pins that are open against the plane of the direction of their removal, but the surgeon should be absolutely certain, before he attempts to make use of such mechanical devices, that the point of the safety-pin is not embedded, either originally or as a result of purposeful disengagement.

**ABSCCESS OF ESOPHAGUS.**—Two cases of large abscesses at the upper end of the esophagus are reported by J. H. Foster (Texas State J. Med. 30: 322 (Sept.) 1934). One case yielded to **drainage** inside, while the other was drained through the neck. Also, 2 cases of abscess in the thoracic portion of the esophagus in which recovery resulted after a slow convalescence without external operation. One death from mediastinitis in the series occurred in a patient too near death for any operative work to save.

**TUMORS OF ESOPHAGUS.—Benign.**—Benign tumors of the esophagus are usually without subjective symptoms and discovered as incidental findings at autopsy. R. Kramer (Ann Otol, Rhin. and Laryng. 43:881 (Sept.) 1934) reports that he has found 36 cases in the literature of lipoma of the hypopharynx and esophagus. In his own patient, the symptoms were tickling sensation in the throat on swallowing of 3 months' duration (male, aged 57). Under suspension laryngoscopy, a fibrolipoma was removed from the submucosa of the right arytenoid and pyriform sinus areas; another was removed 2 years later from the left side of the esophageal introitus; a third is still present in the form of a sessile ridge on the right side of the upper third of the esophagus, 2 inches in length. The latter is producing no symptoms

**Malignant.**—X-ray therapy of carcinoma of the esophagus has not been proven to be successful for obvious anatomical reasons. On the basis of having treated 89 cases by radiation, F. J. Clemmison and J. P. Monkhouse (J. Laryng and Otol 49:313 (May) 1934) raise the basic problem of stimulating effects of radiation on neoplasms. Certainly, radon applied to the center of the growth does not offer a sufficient range of destructive action. It is logical to assume that in these cases stimulation of the growth takes place at its periphery, thereby hastening the patient's end rather than delaying it. Until more effective methods of radiation for esophageal carcinomatosis are developed, these thoughts should be kept in mind, patients' lives may be increased relatively in duration by early **gastrostomy**.

F. L. Lederer (Arch Phys Therapy 15:517 (Sept), 608 (Oct) 1934) states that in malignant lesions of the laryngopharynx and esophagus, surgical intervention, x-ray and radium, alone or when used in combination, have been unsuccessful procedures. **Gastrostomy**, early, is a humane procedure which permits of any type radical therapy thereafter.

**SURGICAL TREATMENT**—When carcinoma of the esophagus is successfully removed the report of such an operation deserves widespread repetition. G. Turner (*Ibid.*, p. 297) performed the "pull through" operation on a man, aged 58, under general anesthesia. Three weeks prior, a **preliminary gastrostomy** had been done, and the liver explored. The 4 steps in the removal of the esophagus were:

(1) The abdomen was reopened through a middle line incision carried high up between the left costal margin and the xyphisternum. The left lobe of the liver was detached from the diaphragm and turned to the right, exposing the abdominal portion of the esophagus. A quantity of 0.05 per cent solution of **procaine hydrochloride** was then injected around the lower thoracic portion of the esophagus, to distend the cellular spaces around it and to displace the pleura. The peritoneum over the esophagus was incised, and the enucleation was commenced by the forefinger introduced through the hiatus and worked up as far as possible around the tube. (2) A transverse or oblique incision was made first above the left clavicle, dividing the sternocleidomastoid muscle. The cervical portion of the esophagus was exposed by blunt dissection. The esophagus was then ligated and divided as low down as was feasible, but at least 2 inches (5 cm) above the growth. (3) A return was made to the abdomen, and traction exerted on the esophagus. When it was freed from its bed, it was ligated at the cardia and cut away from the stomach, and the stump securely buried by purse-string sutures. (4) The open esophageal tunnel was closed by suturing the left lobe of the liver over its mouth, and the abdomen closed. This procedure was followed fairly



closely, and the patient had a smooth postoperative course. Later, a neoesophagus was fashioned from a skin tube over the front of the chest and a loop of jejunum connecting this tube with the stomach.

In spite of many failures, Turner believes that the radical surgical intervention holds some promise. It is better not to attempt the repair of the esophagus *in situ*, but after recovery to supply the defect by making a **new esophagus** by the anterior route. For a growth of the upper end he suggests an excision with formation of a cervical fistula and completion of a new esophagus. For a growth of the lower end, the plan outlined is recommended, but for a tumor of the middle portion he believes that further consideration should be given to operation by the posterior mediastinal or transthoracic route.

**DIPHTHERIA.**—In discussing the *results of surgery* in diphtheria, C. W. Bailey (Arch Otolaryng. 20:162 (Aug.) 1934) states that he has never seen a fatality occur in any of the cases he has observed that had previously had either a tonsillectomy and adenoidectomy performed or had at some time previously been actively immunized and later proved to have a negative reaction to the Schick test. None of the patients with obstruction of the lower part of the pharynx requiring a tracheotomy completely recovered. They usually died of myocarditis. Direct laryngoscopies, in addition to the routine examinations, were performed on all patients who exhibited a croupy cough or any degree of labored respiration.

It is of interest to note that Bailey has not observed mucosal bleeding following the *removal of a pseudomembrane from the larynx*. He states that bleeding occurs in instances of removing membranes from the tonsils because of their great vascularity. Instead of passing a bronchoscope for the removal of tracheal secretions, a blunt 20 or 40 cm aspirating tube is used through an anterior commissure laryngoscope. This is obviously a logical improvement in the technic in an attempt to avoid trauma to the inflamed laryngeal mucosa and to avoid the production of subglottic edemas. In addition, such a procedure facilitates speedy peroral manipulations. Casts may involve separately any region of the tracheobronchial tree, larynx or pharynx. Since the pseudomembrane usually reforms within 12 to 24 hours, reaspiration is required in many cases. The foregoing eliminates to a great extent the insertion of the *O'Dwyer tube and its dangers*, which are:

1. In a child who has had intubation done an emergency is always likely to occur, for the tube may be coughed up at any time, leaving the larynx in spasmodic stenosis and requiring immediate reinsertion of the tube to prevent sudden death from asphyxiation.

2. When intubation is done without first cleaning the membrane from the larynx, the membrane may be pushed down in front of or into the tube, thus blocking the lumen. Also, when the membrane has not been cleaned from the trachea and large bronchi before intubation, the cast may break away and be coughed against the distal end of the tube, blocking the opening. Either causes an emergency requiring immediate extubation, clearing of the larynx and trachea, and possibly reintubation with a clean tube.

3. Intubation, when done by the most skillful operators, sometimes traumatizes the inflamed laryngeal mucosa. This almost always happens when intubation is done by beginners. The traumatized area, depending somewhat on its extent and the resistance of the patient, may heal primarily without infection, or it may become infected and form an ulcer. When once an ulcer forms, such a larynx almost always becomes spasmodic when the tube is removed, often to the extent of producing complete stenosis requiring immediate reintubation and subsequent treatment of a "chronic tube case."

4. Even when a perfect intubation has been performed without trauma, and the tube has been left in for a few days, it always acts as a foreign body to the larynx, and ulceration may form about it. This rarely happens, but when it does, there is a potential "chronic tube case" to deal with. And even in the "chronic tube case" after the patient is freed from the tube there is always a certain amount of cicatricial stenosis resulting, which may or may not completely clear up.

5. When intubation causes ulceration and secondary infection in the larynx, it greatly increases the possibility and danger of secondary bronchitis and bronchopneumonia.

The following *technic to facilitate control of intubation tubes* has been employed by Bailey (*Ibid.*). In using O'Dwyer's intubation tubes in emergency cases, No. 4 banjo wire is securely attached in the hole in the shoulder of the tube. After the tube is inserted into the larynx the wire is cut, so as to leave the ends free in the roof of the mouth, making it impossible for the child to work the tube out with his tongue. Also, this makes it easy to perform extubation quickly. Splints are put on the child's elbows, so that it is impossible for him to take out the tube with his hands. The tube is ordinarily left in the larynx for 5 days, after which it is removed and left out if possible. In selecting a day for extubation, the weather should be considered. If possible it should be a bright sunny morning, for it has been proved by experience that children from whom the tube has been removed on a damp rainy day more often require reintubation.

Diphtheria of the lower alveoli of the lungs, termed *diphtheritic bronchopneumonia*, is a type of diphtheria of the lower respiratory tract that is always fatal, since no procedure has been devised to relieve it. It is usually associated with tracheobronchial diphtheria, but Bailey has seen it occur independent of involvement of the larynx, trachea and upper bronchi. As soon as the membrane begins to soften and liquefy, the terminal bronchioles become obstructed with fluid and the child soon suffocates. The diagnosis in these cases in Bailey's series was easily proved at autopsy by macroscopic, microscopic and bacteriologic examinations.

Bailey states that the relief of "*chronic tube cases*" has been a serious problem since the invention of the O'Dwyer tubes. However, it is not the problem it was before laryngoscopy and aspiration began to be used. Before that time there was a special building containing 20 beds at the Philadelphia Hospital for Contagious Diseases to care for such cases and for resulting cases requiring tracheotomy. But with the introduction of laryngoscopy and aspiration there are few

obstinate chronic cases. It is safe to say that this procedure alone has eliminated the vast majority of these cases. The condition to be relieved was one of cicatricial stenosis, either of a small portion of the larynx or of the whole of it.

The method of relieving these patients is, first, to try to insert a tube 1 or 2 sizes larger in diameter than the original tube but of the same length. Usually the patient can retain this tube for from 2 to 4 weeks without an elevation of temperature. Then it can be removed without producing spasmodic stenosis sufficient to require its reinsertion. Only hard rubber tubes are used because they are much lighter and cause less reaction of the tissue. When the tube can be kept out by this method for 2 days, nature and normal use of the larynx will complete the recovery. When this method fails to give results early, low tracheotomy should be resorted to without further delay. Then the laryngeal tube is removed and the patient is soon made to breathe through the larynx by gradually plugging the tracheotomy tube. As soon as it has been completely plugged for 3 or 4 days and the patient is doing well, the tracheotomy tube is removed and the wound closed.

Only two conditions remain today that necessitate a **tracheotomy**, *i. e.*, the pharyngeal obstruction caused by excessive cervical edema, and the few "chronic tube cases" that require it. It is not often done for the relief of acute laryngeal diphtheria, but it is sometimes the safest procedure for a patient who must remain at home or far out in the country or who is far away from one trained in laryngoscopy and aspiration and intubation. An orderly low tracheotomy is much safer than intubation without preliminary laryngoscopy and aspiration, and far better and safer than leaving the intubated patient unprotected at home. Emergency tracheotomies in small children are considered dangerous by those who have had experience in doing them, and should be prevented if possible. They may be avoided in cases of laryngeal obstruction if the operator has any kind of laryngeal tube that may be temporarily inserted, and in cases of pharyngeal obstruction if the operator has a laryngoscope, bronchoscope or similar tube that may be used temporarily to force an opening through the pharynx until an orderly tracheotomy is done.

*Abscess of the lung* is an infrequent sequel to diphtheria of the lower respiratory tract, only 2 cases being observed in my series. One was a girl of 10 years, who had extensive diphtheritic involvement of the throat and lower respiratory tract. Laryngoscopy and aspiration were done several times during the first 4 days in the hospital before the larynx remained free from pseudomembrane. Then during the third week of convalescence a small abscess was found in the lower lobe of the right lung. It was treated 7 times by **postural drainage** and by **bronchoscopic aspiration**. The abscess soon cleared up and the child was discharged to the care of her family physician. The other abscess was in a boy of 13 who had a similar diphtheritic involvement. An abscess in the lower lobe of the right lung developed during the third week of convalescence, but cleared up after 3 **bronchoscopic aspirations**. Intubation was not done in either case. The diphtheria bacillus could not be recovered from aspirated pus, although staphylococci were obtained in pure culture. Possibly many other minute abscesses developed on the lungs and cleared up spontaneously.

In Philadelphia the law requires for *release from quarantine* the obtaining of 2 successive negative cultures from both the nose and throat and also from any abnormal discharge. Once, for experimental purposes the writer took a third culture in 100 successive cases after the two successive negative cultures required for discharge had been obtained. In 63, the third culture was positive; therefore, the logical conclusion would be that the law should require the removal or recovery of any apparent harbor of the bacillus.

The principle followed in relieving the patients is **extirpation of the focus of infection** when possible, and adequately opening for **drainage** the foci that could not be extirpated. Bailey does not consider it radical to say that the **tonsils** and **adenoids** should be **removed** as a routine in every case after recovery from the acute disease; for even though no bacilli are found by a culture from the nose and throat, they are usually present in the crypts of the tonsils and adenoids. Also, the tonsils and adenoids have been affected beyond repair by the diphtheria bacillus and the mixed infection which always accompanies it, and should be removed.

When *positive cultures* are obtained from the nose, the nasal mucosa should be kept reduced by a spray of 2 per cent aqueous **solution of ephedrine sulphate** or **ephedrine hydrochloride**, so that free ventilation and drainage are not obstructed. Also, the nostrils should be irrigated once or twice a day with a **Lore nasal irrigator**, using **physiologic solution of sodium chloride**. If positive cultures persist after a week or 10 days of treatment, it should be assumed that the foci of infection are in the accessory nasal sinuses. Inspection of the nasal passages and transillumination will usually indicate the *infected sinus*, but often x-ray examination and even direct irrigation of the sinuses are necessary to make the diagnosis. An **intranasal operation** to permit drainage should be performed. After all foci of infection are removed or drained, it is well to use **germicide solutions in the nose and throat** and for direct **irrigation of the sinuses**. When pus draining from an ear gives a positive culture for diphtheria bacilli a secondary infection is always present. The treatment is that ordinarily indicated in the absence of diphtheria bacilli. However, the assumption is made that no discharge should be allowed to flow for more than 3 to 6 weeks without surgical intervention.

**TUBERCULOSIS OF LARYNX.**—*Treatment*—F. L. Lederer and L. Z. Fishman (Illinois M. J. 66, 448 (Nov.) 1934) begin their attack on the problems of laryngeal tuberculosis by asking the pertinent question, "Is laryngology arriving at or is it passing the stage of adolescence?" They continue, "Considering all things relatively, we are not so certain that laryngology, particularly the subject of laryngeal tuberculosis, is as familiar to many of us as it is entitled to be. This statement regarding the subject under discussion is not made on the basis of fancy, but upon that of the palpable lack of available information which is shown by present-day publications concerning tuberculous disease of the larynx, particularly its therapy."

It has always appeared to the writers that there has been a laxity in the treatment of this affection, first, through the lack of understanding of the disease, and, second, because of a phlegmatic or pessimistic attitude in regard to this

complication The fatalistic attitude of many physicians of past decades regarding the incurability of laryngeal tuberculosis, is not as prevalent as formerly, although there are still those who could be living in that period, preceding 1880, before the advent of rational therapy of the larynx. The treatment since has varied from one extreme of passive and hopeless expectancy to the other of energetic surgical interference. Many of the methods that have been recommended are successful in some hands, but have failed in others because of improper technic and the lack of individualization regarding the choice of cases. The ease with which these errors are committed may be demonstrated in a vivid manner by pointing only to the wide variations in certain conceptions regarding this disease. For example, specific involvement of the larynx in pulmonary cases varies in occurrence from 3 to 97 per cent. in the statistics, according to their source; in the average variety of cases, 3 to 25 per cent. would more nearly approach a correct statistical figure. In their own institutional experience Lederer and Fishman find that 15 per cent. of patients with pulmonary tuberculosis have laryngeal tuberculosis. To treat all cases regardless of lung pathology and type of laryngeal involvement by universally applying one form of therapy is obviously unfair, even in the light of good results. Reports are being published recommending one or another form of therapy as a routine procedure in all cases of laryngeal tuberculosis. They look upon this lack of discrimination as being illogical, and consider it to be of greatest importance, in reporting a type of therapy, to indicate in no uncertain terms the method according to its separate and individual indications.

#### PROPHYLAXIS IN THE TUBERCULOUS

- 1 A high standard of the patient's physical and mental status must be maintained

- 2 The larynx must be examined frequently in all cases of tuberculosis, as much depends upon early detection of local pathologic processes. Attention must be directed to the minor laryngeal complaints before they attain major proportions

- 3 Local areas, when nontuberculous, must be treated to prevent the resistance of the parts from becoming lowered. Chronic laryngitis must be treated as well as abrasions and superficial ulcerations.

- 4 Voice hygiene or absolute vocal rest is important. Proper use of the voice is to be emphasized, especially for those who are subjected to coughing paroxysms which alone punish sufficiently the vital components of the larynx.

- 5 The so-called "common cold" particularly should be watched and properly treated

#### OBJECTIVE OF ACTIVE TREATMENT

- 1 To relieve symptoms which not only interfere with comfort but also defeat one of the main objectives in the general treatment, *viz.*, nutrition

2. To obtain complete arrest of the tuberculous infection, pulmonary and laryngeal.

3. To cure it in the larynx, preserving, if possible, laryngeal function

## OUTLINE OF ACTIVE TREATMENT.

1 *Drugs.*

- (a) Intralaryngeal Instillations or Sprays. Chaulmoogra oil, mentholated oils, orthoform emulsions, cocaine, butyn
- (b) Topical Applications Formalin, lactic acid
- (c) Insufflation of Powder Orthoform, thioform, methyl violet, iodoform, anesthesin, zinc stearate.
- (d) Inhalation of Vapors. Benzoin, menthol, creosote, guaiacol.
- (e) Lozenges: Orthoform, anesthesin.

2 *Heliotherapy and Radiotherapy*

- (a) Finsen light (carbon arc).
- (b) Direct reflected sunlight
- (c) Ultraviolet
- (d) X-ray.
- (e) Radium.

3 *Cautery.*

- (a) Thermo- or Electrocautery: Galvanocautery, surgical diathermia
- (b) Chemical Cautery Trichloroacetic acid, neutral quinine hydrochloride, lactic acid, formol, paramonochlorophenol, formaldehyde, and silver nitrate

4 *Surgery*

- (a) Endolaryngeal and Extralaryngeal Procedures Curettage and scarification, tracheotomy, epiglottidectomy, superior laryngeal nerve blocking and resection, thyrotomy, laryngotomy, hemilaryngectomy, laryngectomy
- (b) General Surgical Procedures Collapse therapy, resection of phrenic nerve, extrapleural thoracoplasty, gastrostomy, etc

**TUMORS OF LARYNX.—Benign Tumors.**—*Amyloid disease* of the upper air passages is classified clinically into 3 types (1) diffuse subepithelial infiltration, (2) tumor forming local amyloid deposits, and (3) amyloid degeneration of preexisting tumors. J. O. Beavis (Arch Otolaryng 19:439 (Apr) 1934) adds 5 cases, all occurring in males, to the 50 cases appearing in the literature. The *diagnosis* is difficult to make clinically until examination of biopsy material is completed. The *treatment* must first be directed at the causative pathology. Local therapy is limited, when the larynx is involved, to establishing its patency and restoring the voice by **surgical removal**. **Fulguration and radium preceded by thyrotomy** is of value in diffuse growths, while little is known concerning the efficacy of x-ray therapy.

**Malignant Tumors.**—F. L. Lederer (Arch Phys Therapy 15:517 (Sept), 608 (Oct) 1934) makes glaring the faults of many reports which deal with the problems of *cancer*, such as, "the preaching of radicalism and practicing of conservatism, and preliminary reports which are never confirmed or denied later."

**STATISTICS**—In general, these are of value, but critical analyses from them may not be obtained or advanced to support ideas as to frequency and incidence. E. Fischel (Am J Surg 24:711 (June) 1934) words the same thoughts as Lederer in another manner. "When one peruses the numberless articles which

concern themselves with treatment, however, one meets with most divergent statements, opinions and figures. Can it be that abstract studies are undertaken in a more scientific manner by better trained scientists more capable of arrival at the truth, or is lack of agreement as to treatment due not only to careless handling of material, but also to the desire to be first in the field of a new and better therapy either for prestige or for financial profit? Sometimes I am forced to the belief that many of the writers of statistical studies of cancer are either woefully ignorant or wilfully blind."

CLASSIFICATION.—In laryngeal cancer, this is made primarily on the basis of anatomic location. The reasons for such a classification are more fundamental than would appear from this casual statement. As Lederer (*loc cit.*) states, first, the enclosure of the laryngeal cartilages, and second, the lymphatic drainage, which is not as extensive from within these cartilages as from without, provide for the division of neoplastic lesions into 2 main groups:

- 1 *Intrinsic*, identifying growths on or below the true cords,
- 2 *Extrinsic*, identifying growths anywhere above this level (false cords, the arytenoids, aryepiglottic folds and pyriform sinus—most frequent site in malignancy of the hypopharynx).

The *intrinsic* types are slow-growing and metastasize late; if diagnosed early, these lend themselves to surgical eradication. The *extrinsic* types are characterized by early and ready metastases by way of the rich lymphatics of these regions into the extensive lymph nodes of the neck. Such lesions are therefore considered to be inoperable. Lederer states further that his observations of laryngeal cancer have been an incredulous nightmare because less than 2 per cent of the cases have been intrinsic, and, therefore, operable.

ETIOLOGY.—The *factor of vocal abuse* in the development of laryngeal cancer is not entirely acceptable. Nevertheless, constant laryngeal irritation, by whatever agents, provides a potentially precancerous condition in a person in the so-called cancer age, which means, according to Lederer (*loc cit.*), "anyone under sixty!" He emphasizes the common finding in his cases of poor dental hygiene. Regarding the rôle of smoking, Hoffman is quoted who noted that the incidence of laryngeal cancer is great among Tyrol women who smoke considerably. Yet, to show how inconstant this etiologic factor is, Lederer cites 4 of his own cases of laryngeal carcinoma in women who had never smoked. It must be remembered, consequently, that there appears to be no direct relation between the pathology of carcinoma and the biological reactions of such processes.

PATHOLOGY.—*Microscopic* characteristics are important, too, in determining the malignancy-potential of a growth. The anaplastic, immature types are radiosensitive, metastasize extensively, are fast-growing but later become radioresistant and destroy the host, irrespective of therapy, if the growth is not completely destroyed early. The more mature types of carcinoma characterized by pearl formations are radioresistant, metastasize late and are slow-growing, thereby permitting successful eradication surgically if diagnosed early. The latter make up the greater number of cases of intrinsic cancer of the larynx.

Multiple malignant tumors of primary nature are, in contrast to multiple benign tumors, comparatively rare (Lederer quoting R. Luchsinger: Ztschr. f. Path. 40:417 (Nov.) 1933). Such primary multiple tumors may be divided into several groups, *i. e.*: (1) those which are found in the same system; (2) those which are found in organs that have a physiologic relationship; and (3) those which appear in organs not having any relationship to one another. Lederer cites

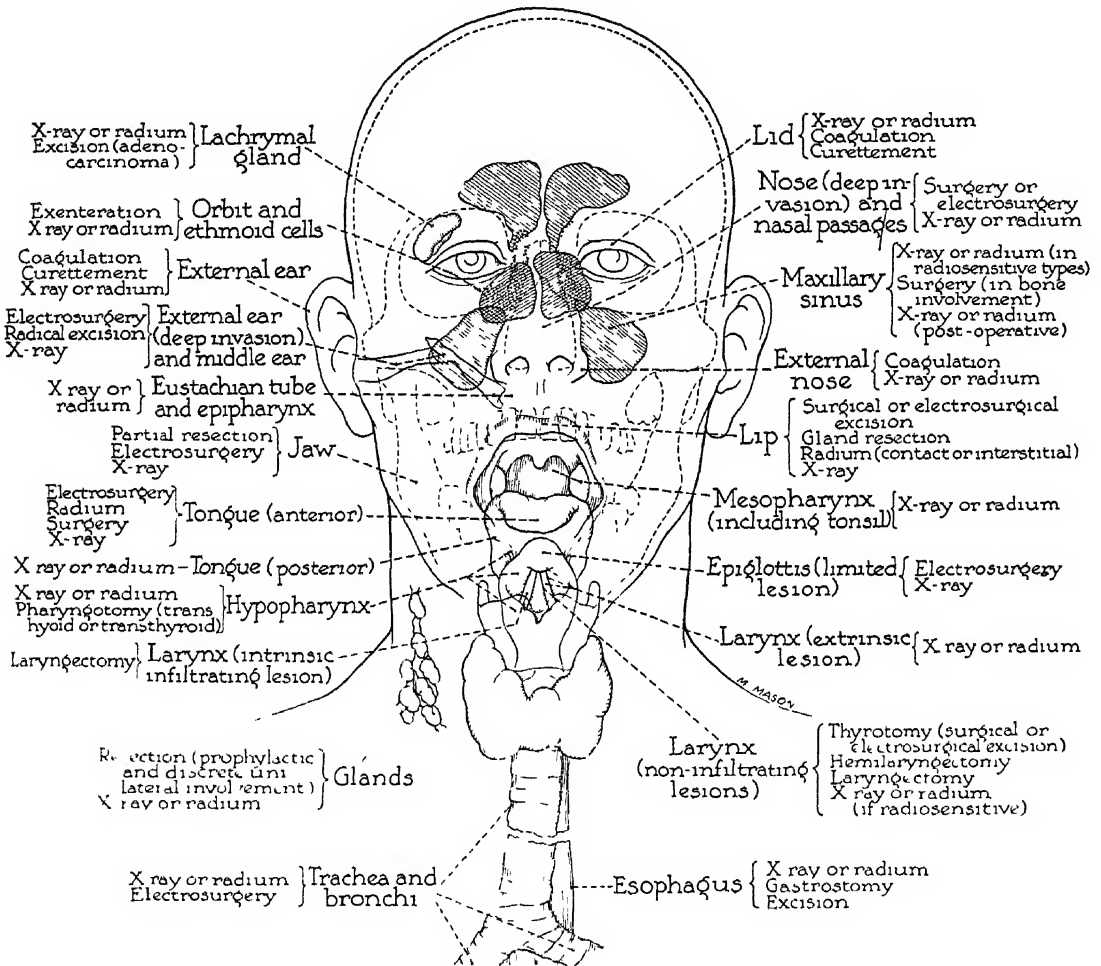


Fig 1—Regional distribution of cancer, showing most logical modes of attack in various locations, in order of their proven value. Some may be used singly, others in sequence or in combination depending, of course, upon the type of cellular activity, depth of involvement and character of tissue invaded (F L. Lederer, 1934)

a case belonging to type (3), of squamous carcinoma of the larynx and of the skin, following trauma, of both hands

COMPLICATIONS—*Cervical Lymphadenopathy*—Lederer (*loc. cit.*) states, "It is well to remember, when we speak of glands, that glands in the neck are not always secondary malignant manifestations, especially those that are discrete and small. For example, in the large majority of cases of carcinoma of the tongue and floor of the mouth, the salivary glands that can often be palpated are not the seat of carcinoma. The enlargement is frequently of a chronic inflamma-



tory nature, apparently due to infection carried along the ducts from the mouth." E. Fischel (*loc. cit.*) has demonstrated without doubt that palpable lymph nodes of the neck in carcinomatosis may be nonmalignant and only hyperplastic; the reverse was found to be true also, *viz.*, metastases to lymph nodes are not necessarily made evident by enlargement of these nodes. These observations are based on microscopic studies of specimens removed surgically and at autopsy. Finally, Fischel states that conclusive evidence that any method other than surgery is effective either in the prevention or the cure of cervical metastasis is lacking. In

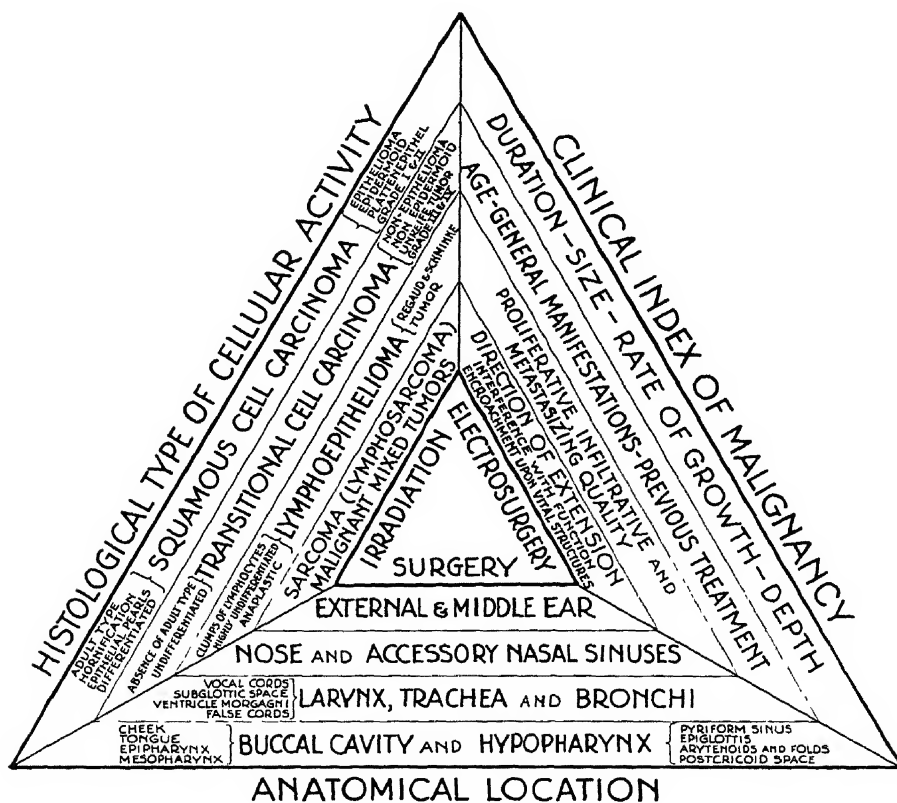


Fig. 2—Schematic representation of bases for rationalizing indications for therapy in cancer. The triad of therapy, *viz.*, surgery, irradiation and electrosurgery, singly or in combination, is indicated with a consideration of all these factors. (F. L. Lederer, 1934)

the cases studied in the report which showed proved carcinoma in the lymph nodes, in 33 per cent of the lip cases and 13.8 per cent of the mouth cases the patients lived 5 years or more after operation. Accordingly, Fischel concludes that the **resection of lymph nodes** as an important part in the routine treatment of carcinoma of the lip and buccal cavity is to be strongly advocated. [The evaluation of metastases from these regions may be estimated in a similar manner in the considerations of metastases from laryngeal cancer—EDITOR]

**DIAGNOSIS.**—*Clinical Index of Malignancy*.—Although Lederer (*loc. cit.*) states that there is no stereotyped manner of judging malignancy, he presents the accompanying chart (Fig. 2) merely as an aid in an attempt to arrive at such

an index. Facts gathered according to such a scheme may then be evaluated with a great degree of certainty in rationalizing prognosis and therapy.

Simple rules for grading malignancies, such as the plan of A. C. Broders (Minnesota Med 8:726 (Dec.) 1925) have not served their intended purpose. Lederer quotes Riemann particularly as having found only 5 per cent of his cases corresponding in their course to the prognosis rendered on the basis of Broders' histological grading.

*Biopsies* are always essential to therapy. They are not always authoritative, however, and should be repeated if there is the least suspicion of malignancy. Lederer (*loc. cit*) warns against the fear of producing metastases as the result of such a diagnostic procedure. He states that such fears are ill-founded; he has never seen metastases result from biopsy performed a long time prior to the operation. The procedure of some clinicians who insist that biopsy be performed with the understanding that, if findings are positive, the patient be immediately prepared for surgery or for other indicated surgery, appears sound to Lederer. Coexisting growths as osteogenic sarcoma associated with Paget's disease, lupus, plasma cell granuloma, gummata, etc., must always confuse microscopic studies of neoplasma.

**PROGNOSIS**—A patient is considered as cured from neoplastic disease by C Jackson (Surg Gynec Obst 58:431 (Feb 15) 1934) if there is no recurrence 5 years after removal of the growth. He feels that thereafter, the appearance of a new growth, even at or near the same location, indicates a new process. In a series of 74 cases of carcinoma of the larynx operated upon by laryngofissure prior to 5 years ago, Jackson reports 41, or 55.4 per cent, as being alive and well 5 or more years; 9 died of recurrence before the end of 5 years, 2 died of cancer of other regions without local recurrence, 3 died of disease other than cancer within 5 years, and 19 were untraceable after 1 year.

**TREATMENT, NONSURGICAL**—An interesting summary of nonsurgical methods in the treatment of malignancy in the last 20 years presented by Lederer (*loc. cit*) shows the great mystery under which this disease still lives today. This situation exists despite the ever-increasing amount of medical knowledge. It is appropriate to present such an historical outline as the following which Lederer has constructed:

- I. Bacteriotherapy.
  - Bacterial products.
- II. Autoserotherapy and Organotherapy.
  - Autolytic solutions (tumor extracts or specific globulins or proteins).
  - Proteins (nonspecific).
  - Autohemotherapy.
  - Vaccines.
  - Serous exudates.
  - Tissue extracts: Cartilage, muscle, hematopoietic tissue (bone-marrow, blood, thymus and spleen), liver, pancreas, embryonal and placental tissue.
  - Physiological or endocrine therapy.
    - Pituitary, thyroid and parathyroid, suprarenals and gonads.

III. Vitaminotherapy.

IV. Chemotherapy :

- |                              |                                             |
|------------------------------|---------------------------------------------|
| 1. Escharotics externally :  | Silicon.                                    |
| Arsenic paste.               | Gold.                                       |
| Arsenic-mercury paste.       | Strontium.                                  |
| Chromic acid.                | Mercury.                                    |
| Trichloracetic acid.         | Thorium.                                    |
| Butyric acid.                | Selenium.                                   |
| 2 Arsenicals internally:     | 4 Emanations and Radioactive Substances:    |
| Salvarsan.                   | Solutions.                                  |
| Atoxyl (arsenic and anilin). | Alphacatalyst                               |
| 3 Elements (colloidal):      | Choline.                                    |
| Copper.                      | 5. Dyes:                                    |
| Magnesium.                   | Trypan red.                                 |
| Zinc.                        | Trypan blue.                                |
| Iron.                        | Trypaflavine.                               |
| Lead.                        | Congo red.                                  |
| Antimony.                    | Eosinate of selenium.                       |
| Potassium.                   | Methylene blue.                             |
| Arsenic.                     | Scheele green.                              |
| Calcium.                     | Pyrrol blue.                                |
| Silver.                      | Isamine blue.                               |
| Bismuth.                     | 6. Acid therapy :                           |
| Uranium.                     | Hydrochloric acid, oxygen and nitrous oxide |
| Platinum.                    | 7. Carbon dioxide snow.                     |

V. Physical Methods:

1. Irradiation
  - (a) X-ray
    - Skin therapy (50,000 to 100,000 volts)
    - Superficial therapy (50,000 to 140,000 volts).
    - Deep therapy (200,000 volts).
    - Super therapy (500,000 to 1,000,000 volts).
  - (b) Radium:
    1. The element.
      - Capsules, superficial collar application.
      - Needles—Intratumor or interstitial implantation.
      - Superficial contact or surface application.
    - 2 The emanations
      - Radon seeds, interstitial implantation.
    - 3 The pack or horn—telerradium application
- 2 Electrosurgery (Surgical Diathermy)
  - Cutting current (Biterminal and monoterminial high frequency current)
  - Obtained from the primary winding of the high frequency transformer
  - Electrodesiccation (including Fulguration) (Monoterminial high frequency current) From the secondary winding of the high frequency.
  - Electrocoagulation (Biterminal and monoterminial high frequency current)

*Irradiation, Delayed Effects*—K Vogel (Ztschr f Laryng, Rhin, Otol 24 172 (May) 1933, Arch Otolaryng 18 6 (Dec) 1933) reports that 4 patients with laryngitis sicca, and superficial ulceration of the vocal cords, had received x-ray or radium irradiation from 2 to 14 years previously in 1 case for laryngeal carcinoma, in 2 cases for tuberculous cervical lymphadenitis and in 1 case for cervical lymphomatosis Vogel believes that the irradiation therapy

decreased the resistance of the vocal cords to catarrhal infections and produced a tendency to dry laryngitis with torpid superficial ulceration; this is analogous to the acute necrosis of the laryngeal cartilage in irradiated patients. In the patients irradiated in early childhood, hypoplasia of the larynx, in one case producing spontaneous stridor, was noted; also cicatricial hypoplasia of the soft parts of the neck and the inferior maxilla of the irradiated side. Vascular ectasia was seen in the true vocal cords in one case and in the false vocal cords in another case.

*Electrosurgery.*—Lederer (*loc cit.*) states that **surgical endothermy** possesses many advantages when used in the dissection and destruction of malignant tissue. For producing hemostasis and sterilization of tissue and for reducing the danger of metastasis in the course of surgical procedures it has also proved its merits. Followed by radiotherapy, it is of great usefulness. There is little or no shock. The disadvantages, *i. e.*, that it is not selective in its destructive actions and that there is danger of secondary hemorrhage, are not sufficient to outweigh its general usefulness. Occasionally there is observed, however, extensive sloughing with severe pain and toxemia. Before electrocoagulation of large masses of tissue is undertaken, the larger blood-vessels must be tied off if accidents are to be prevented. In managing tumors of the pharynx, ligation of the external carotid should be a preliminary measure.

*Surgery.*—If anything of a noteworthy character can be written in the annals of surgical advance, it is in regard to **total laryngectomy** in intrinsic carcinoma of the larynx, according to Lederer (*loc cit.*). After many years of failure, in a large number of cases, due to infection, secondary hemorrhage, postoperative sepsis and bronchopneumonia, this very formidable procedure has reached the stage where the percentage of failure has been reduced to almost a negligible figure. Early diagnosis, resulting from improved and simplified methods of diagnosis—in addition to improved operative technique and a better interpretation of the operative risk—have contributed to the success of laryngectomy.

*Anesthesia.*—With regard to the use of anesthesia, Lederer (*loc cit.*) states that this is a subject which has for years been of great interest. The attention has been directed chiefly on the rectal administration of anesthetic agents, primarily because this method greatly facilitates the operative procedure by avoiding the necessity of an anesthetist and the conflict of his presence in the head area. Another reason for avoiding the use of general anesthesia is the current use of electrosurgical apparatus at the time of operation. While accidents are not common, the possibility of this hazard is obvious enough to have it in mind. **Local** and **rectal** forms of **anesthesia** should be employed wherever possible. During the past 5 years he has been using **tribromethanol (avertin)**.

*Rehabilitation—Development of Speech.*—The sentimental attitude that has existed in previous years in respect to voice deprivation in laryngectomy should not exist today in the face of the facts that have been stated, according to Lederer (*loc. cit.*). Furthermore, the voiceless person may be helped by an apparatus; he may even be **taught to speak without a larynx**. The readiness with which patients take to the latter method, avoiding the conspicuous, if not unnatural sounding, artificial larynx, has been the source of most agreeable surprise. All

patients, of course, learn by intuition the method of speech which is ascribed to a gastro-bucco-esophageal phenomenon, but not all develop intelligible speech. Some very brilliant results are obtained in this direction; these are due mainly to the personal energy and persistence of the patient in systematic efforts in perfecting this type of speech. The development of a simplified **artificial larynx** makes the problem even less difficult for some laryngectomized patients. A number of inexpensive but effective larynges are available. The anatomy, physiology, and development of speech in laryngectomized persons is considered by L. A. Kallen (Arch. Otolaryng 20:460 (Oct.) 1934).

**TRACHEAL TUBERCULOSIS.**—This is not uncommon, but tuberculous disease of the trachea leading ultimately to *suffocation*, as stated in the conclusions of M. McConkey (Am. Rev. Tuberc. 30:307 (Sept.) 1934), is decidedly “a rare complication of pulmonary tuberculosis.” Despite the x-ray evidence of bronchial obstruction, and the patient’s slow exitus (duration 2 hours) from suffocation, no bronchoscopy was performed. McConkey adds that bronchoscopic treatments might have relieved the patient, at least temporarily.

**LIPIODOLIZING OF LUNGS.**—*Technic.*—The technic for inserting a catheter into the trachea and bronchi by the indirect method *via* the nasal route is reviewed by N. Fox and J. W. Harned (Arch. Otolaryng. 18:819 (Dec.) 1933). Of great interest is their “common sense” method of rendering the tip of catheter more radiopaque than otherwise by inserting an ordinary pin into the distal end and anchoring it firmly into the wall of 12 and 16 French soft rubber catheters. This practical device also permits the operator to change the natural curve of the solid tip of the catheter. The technic of insertion is as follows.

Several cubic centimeters of 5 per cent cocaine is dropped into the nostril and allowed to run down into the pharynx, the patient being warned against swallowing the material. After a lapse of 5 minutes, a few drops of 10 per cent cocaine are applied to the cords by a tampon. After waiting for another 5 minutes, 5 c.c. of a 2 per cent solution of cocaine is distributed through the cords to the trachea and the main bronchi. The catheter is fed through the nose, past the epiglottis, into the larynx. The curve of the tip is controlled by manipulation of the nasal portion of the catheter. As it passes the tip of the epiglottis under the guidance of the laryngeal mirror, it is rotated and allowed to enter between the cords. The cords must be thoroughly cocaineized to allow this. After passage into the trachea, the patient is placed in front of the fluoroscopic screen, and by rotation of the nasal portion of the catheter, it is gradually fished into the area desired. With a small amount of practice, one can quickly pick out the bronchus one desires to enter and learn to turn away the tip from bronchi which are not to be entered. After deftness has been gained in manipulating the tube, the upper lobes may be as easily entered as the lower. The catheter is then attached to the ordinary suction pump, and aspiration is accomplished. If it is desired, irrigation and aspiration can be done quickly without flooding other areas, or medication of any desired type can be carried out. In addition, the catheter affords an excellent method of placing radiopaque materials in selected areas. If a fluoroscope is available, the entire procedure may be carried out in the office and the patient dismissed with practically no discomfort.

**FOREIGN BODIES.**—H. J. Hara (Arch. Otolaryng. 20:549 (Oct.) 1934) summarizes the results of experimental studies on the reaction of lung tissue of young rabbits to 10 different solid organic foreign bodies introduced intratracheally by means of peroral endoscopy. (Animals were killed at the end of 24-, 48-, 72-, and 96-hour periods.)

1. The gross appearance of the lungs varied considerably according to the objects introduced, to the manner of bronchial obstruction and to the period of observation which elapsed before the animal was killed. The most intense reaction was noted in lungs containing peanuts, bark of the pepper tree and pop-corn. The seeds of citrous fruits, grapes and watermelon produced a moderate reaction. The least reaction was shown by the bark of the eucalyptus tree and seeds of the cantaloupe.

2. Histologic examination of the lung tissue indicated that the response was progressive, consisting of exudation and proliferation. These two processes went on simultaneously. The exudative reaction consisted of the pouring out of large, swollen, irritated septal cells into the pulmonary alveoli to form an inflammatory alveolar exudate. The proliferative reaction consisted of the multiplication of cells lining the alveoli.

3. The reaction increased with each subsequent day until the pulmonary parenchyma lost its normal architecture. The area of exudate formed was always limited to the immediate neighborhood of the larger bronchi and extended outward. The rapidity with which this expansion took place appeared to be in direct proportion to the degree of irritation.

4. Secondary change in the lungs was always localized pneumonitis, never lobar. This occurred on the fourth day in lungs containing the most irritating foreign bodies.

5. The large mononuclear leukocytes were made the principal proliferating cells. These showed a tendency to form large multinucleated cells, probably precursors of the giant cells. They were shown best in lungs containing grape seed.

6. Vascular change was uniformly that of obliterating arteritis with a foreign body causing a marked reaction. This proliferative change in the endothelial lining of the blood-vessels brought on, successively, infarction and focal necrosis of the pulmonary parenchyma.

7. Frank capillary hemorrhage in the alveolar wall, and to some extent hemorrhage in the alveoli, was noted in lungs containing pop-corn, the bark of the eucalyptus tree, the seeds of the watermelon, grapefruit and orange, and particularly peanuts.

8. Similar changes were noted in the opposite lungs, which contained no foreign bodies.

9. The primary cause of drowned lung is the too rapid and excessive outpourings of mucus and exudate in the presence of a decreased abolished cough reflex.

10. The rapidity of onset and subsequent clinical symptoms due to the presence of organic foreign bodies in the bronchi have their well defined histologic counterparts during each stage of their development.

**BRONCHIECTASIS.**—That the common cause of bronchiectasis lies in a paranasal sinus focus is again made evident by L. H. Clerf (*Laryngoscope* 44: 568 (July) 1934). In 200 cases of bilateral bronchiectasis, evidence of sinus disease was found in 82.4 per cent. As is common experience, Clerf has found that active treatment of bronchiectasis is at best only palliative. He states that

its prevention is of greater importance. Chronic bronchitis, though the most frequent cause of bronchiectasis, should be looked upon as a secondary disease; here, again, sinus infection plays an important part. He states further that children offer better prognoses under very active and diligent therapy, both local and general, than adults. The reasons are obvious.

**PULMONARY ABSCESS, NONTUBERCULOUS.**—*Treatment.*—A general review of the treatment and management of nontuberculous pulmonary abscess is presented by G. O. Cummings (Arch. Otolaryng. 19:684 (June) 1934). The study comprises a series of 25 consecutive cases. Location of the abscess or abscesses intimates the type of therapy to which they will be most responsive. Abscesses may be peripheral, parenchymal or central. Tuberculosis must always be excluded from the etiology; then fusospirochetal and *Endamæba histolytica* organisms.

Medical therapy consists of (1) basic measures of support, hygiene and drugs; (2) special measures of **drainage** of the tracheobronchial tree by **posture** and **inhalation** of **carbon dioxide**; stimulation of resistance by the administration of **blood transfusions**, **vaccines** and **nonspecific proteins**; (3) specific measures of medication with **arsphenamine**, **emetine**, **hydrochloric acid** and **serum**; compression of the abscess by **artificial pneumothorax** and physical therapy with **ultraviolet irradiation**. These should always be tried before surgical measures are to be considered (Note: The editor would include **bronchoscopic aspiration** and **broncholysis** as an adjunct to medical therapy.)

Pharmaceuticals should be limited to **laxatives**, **cod-liver oil** and **hematinics**. It should be borne in mind that the cough reflex is the watch-dog of the lungs and that a productive cough is desirable. An *irritating cough* is best limited by the judicious use of tablets of  $\frac{1}{4}$  gram (0.016 Gm.) of **codeine sulphate**. Night spells of coughing may be relieved or prevented by **postural drainage** before retiring or when the spasm of coughing occurs. **Sodium perborate** should be used as a *dentifrice* and *mouth wash*. Such conservative measures resulted in 7 complete recoveries (cases 1 to 7). Cummings has found that autogenous vaccines made from material obtained by bronchoscopic aspiration and used in 6 patients of the series (cases 11, 12, 13, 17, 19, and 25), did not give definite results. The same is said regarding nonspecific proteins and other such medicaments. Seven patients showed the presence of fusospirochetal organisms (cases 11, 17, 18, 19, 20 and 25) and were treated with **arsphenamine**; none were cured, but all improved. In none of the cases was the presence of *Endamæba* demonstrated. Following the advice of Voroshilsky's report from Russia regarding cures which resulted from the use of **antistreptococcus serum** in 8 cases of pulmonary abscess (streptococci were the invading organisms), Cummings tried this method in 1 case. The patient (case 10), aged 44, had a parenchymal abscess of unknown etiology in the upper lobe of the left lung. He was doing well under medical treatment and underwent one bronchoscopic aspiration. Examination of the specimen thus obtained revealed a pure culture of hemolytic streptococci. Five days thereafter he was given 6000 units of polyvalent streptococcus serum and 24 hours later he died. No autopsy was obtained, but the author states that death may have been due to an anaphylactic reaction.

In 2 cases, **artificial pneumothorax** was employed: in case 19 adhesions prevented the introduction of the gas, while in case 11 the patient was cured. The latter patient, aged 53, was progressing satisfactorily under basic medical treatment, until he acquired an influenzal cold and began to have a series of pulmonary hemorrhages. Artificial pneumothorax resulted in cessation of the hemoptysis; refills were made weekly for 6 weeks. Six weeks after the last refill was made he was discharged from the hospital. **Bronchoscopic treatment** is of particular value in the aspiration of tenacious secretions, thereby aiding ciliary activity. These were done at intervals of 5 to 7 days. Granulations may be crushed and medication introduced into the abscessed cavity.

Surgical treatment is discussed under the following captions. compression of the abscess by **phrenicectomy**, **thoracoplasty**, **extrathoracic** and **intra-thoracic pneumolysis**, **incision**, **drainage** and **lobectomy**. These are the last lines of defense in the treatment of lung abscesses and should be attempted only after other forms of treatment have failed.

Thoracoplasty was performed on 2 of the patients, with 1 recovery and 1 death. The patient (case 19) who recovered was 10 years of age; an abscess had developed in the parenchyma of the upper lobe of the left lung after a tonsillectomy. Five patients were treated by incision and drainage 4 recovered and 1 died from hemorrhage from the wound. The recovery rate in Cummings series is 83.3 per cent.

**HODGKIN'S DISEASE (INTRAPULMONIC).—Etiology.**—Lymphoblastoma is once more explained etiologically on the basis of any kind of chronic infection by A. U. Desjardins (J. A. M. A. 103:1033 (Oct 6) 1934). He examined and treated between 500 and 600 patients suffering from Hodgkin's disease or lymphosarcoma during the past 14 years. Of interest to the laryngologist is the listing by Desjardins of chronic bronchitis, leading to "lymphoblastomatous hyperplasia" of the lymphoid structures of the mediastinal nodes, which later spreads to groups of nodes in other parts of the body. Twelve cases are cited to illustrate the common occurrence of infection as the background to the lymphoblastomatosis.

Case 1 (girl, aged 15) had involvement of the mediastinal and retroperitoneal nodes, biopsy showed evidence of Hodgkin's disease, history of repeated attacks of tonsillitis, tonsils not removed. Case 6 (aged 44) complained of general pruritus and lymph node enlargements on the left side of her neck. Examination showed marked bilateral enlargement of cervical lymph nodes, moderate enlargement of axillary nodes on both sides, mediastinal lymphadenopathy with moderate bilateral hydrothorax and enlarged retroperitoneal nodes, with general pruritus (excoriations from scratching). Inquiry revealed extensive dental infection. Case 8 (girl, aged 8) gave a history of many attacks of tonsillitis, last attack continued for about 2 weeks, accompanied by continued enlargement of the right tonsil. Biopsy 2 months later revealed severe inflammation, akin to that which accompanies Vincent's infection. By this time (January, 1934) lymphoid hyperplasia had extended to the right cervical nodes, forming a mass 5 by 3 cm. in size. Despite the removal of the right tonsil previous to this examination, by April, 1934, the mass measured 15 by 10 cm. X-ray therapy produced 50 per cent decrease in size in 4 days and complete disappearance in 2 weeks. However, there was a recurrence later, involving the abdominal and mediastinal lymph nodes. Case 12 (male, aged 42) had enlarged abdominal and mediastinal lymph nodes, which disappeared under x-ray therapy. The patient had suffered from marked pyorrhea for years.



Desjardins concludes that patients should not be allowed to harbor indefinitely teeth, tonsils, gall-bladder or other structures which are known to be infected. The importance of this conclusion is all the greater when the ancestors of the patient have been known to have suffered from lymphoid disturbances.

**Classification.**—Hodgkin's disease of the lung is classified by Moolten (Am. J. Cancer 21:253 (June) 1934) primarily as either (1) proliferative, or (2) exudative, though the majority of cases present a combination of both phases. The proliferative phase displays its most characteristic development within the interstitia of the lung; the exudative phase, which also occurs within the interstitia, attains its most pronounced morphological expression within the alveolar air spaces. Accordingly, the following types of intrapulmonic Hodgkin's disease are enumerated:

1. Granulomatous pan-bronchitis and bronchopneumonia (peribronchial form of granulomatous interstitial pneumonia).
2. Granulomatous pleurogenous pneumonia (pleurogenous form of granulomatous interstitial pneumonia).
  - (a) Primary (rare). (Case 8.)
  - (b) Secondary (invasion from adjacent infiltrated structures, *e g.*, mediastinum).
3. Exudative lobar and lobular pneumonia
  - (a) Acute (gelatinous pneumonia).
  - (b) Subacute and chronic (organizing pneumonia).
4. Miliary, submiliary, and multiple isolated nodular lesions (hematogenous, lymphogenous).

Eight cases are discussed, in all of which the common pulmonary lesions of Hodgkin's disease were typified conspicuously by bronchial involvement. Moolten describes the entire substance of the bronchial walls as providing the matrix for the evolution of the granuloma (condition of "pan-bronchitis"). Not infrequently the bronchi were transformed almost entirely into bulky structureless tubes of granuloma. He states that the characteristic involvement of the alveolar walls, granulomatous interstitial alveolitis, relates this disease to tuberculosis and actinomycosis. Lymphosarcoma, too, shows this interstitial infiltration of the alveolar walls. The difference between Hodgkin's and the latter affection is the absence of proliferation of the alveolar epithelium. Tuberculosis and actinomycosis show the same proliferative changes. This adds further toward considering Hodgkin's disease as one associated with an inflammatory rather than a neoplastic process.

The fifth case described is one in which massive polypoid growths, obstructing the lumen of the large bronchi, were associated with Hodgkin's disease. Moolten reports this association as being described for the first time. Case 6 had asymmetrical involvement, the right middle and lower lobes were diseased chiefly, being almost replaced completely by granuloma and an abundance of fibrosis. Case 7 belonged to the proliferative type of Hodgkin's disease, which resembles neoplastic growth so much as to be labeled "Hodgkin's sarcoma." In this case, however, Moolten states that the designation "sarcoma" cannot be said to apply, since, in spite of the anaplastic character of the growing cells, in its manner of spread through the lung tissue, the lesion exhibited none of the special characteristics of a neoplasm, but conformed in a general way to the habit of growth

peculiar to Hodgkin's granuloma. Case 8 is one of atypical involvement of the spleen secondary to moderate intrapulmonary lesion and rather extensive pleural infiltration. The splenic enlargement (weight 1850 grams) consisted in a diffuse hyperplasia of all the splenic elements, with no evidence whatever of the nodule formation which characterizes the usual type of splenic enlargement in Hodgkin's disease. Little is known of this diffuse non-nodular type of splenic hyperplasia.

**X-ray therapy** in these cases either had only slight beneficial effects which were lost later or had no effect on alleviating or arresting the progress of this disease in the foregoing patients. The interest to the clinician must still be one of differential diagnosis leading to rational prognoses; consequently, bronchoscopy is of great value, particularly when bronchi are filled with granulomatous masses.

**TUBERCULOSIS AND CARCINOMA.**—In a period of 14 years of exclusive practice in tuberculosis sanatoria, I D Bronfin (Colorado Med 31 193 (June) 1934) saw only 9 cases of primary carcinoma of the lung, 8 males and 1 female. Among the 6 cases constituting the basis for this report, 4 had symptoms simulating pulmonary tuberculosis, but a more careful clinical analysis might at least have led to a suspicion of malignancy and the necessary diagnostic procedures instituted. In 2 patients there was an associated pulmonary tuberculosis. While preceding inflammatory conditions of the lung, notably influenza and tuberculosis, are considered by many observers as important etiologic factors, this was not borne out by Bronfin's experience.

He concludes that (1) there is no apparent etiological relationship between pulmonary tuberculosis and carcinoma of the lung, (2) the coexistence of active pulmonary tuberculosis with carcinoma is rare, (3) the early differential diagnosis of these two diseases is extremely difficult, (4) x-ray and bronchoscopic examinations are valuable aids in diagnosis but have definite limitations, (5) respiratory symptoms simulating pulmonary tuberculosis in a person past the age of 40, when the physical and x-ray findings are either entirely negative or atypical for tuberculosis, warrant a tentative diagnosis of malignancy until proved otherwise.

R H Kampmeier and H A Black (Am Rev Tuberc 30:315 (Sept) 1934) report a case of *aspergillosis* occurring in the presence of a *bronchial carcinoma*. They made the diagnosis, tentatively at first, on the history and physical examination. However, some doubt was cast by the constant presence of the *aspergillus* in the sputum without tubercle bacilli. The x-ray shadow in the left lower lobe could not be satisfactorily explained on the basis of bronchogenic malignant tumor as could the hilus shadow, which was compatible with such a diagnosis. The fact that the shadow of the lower lobe cleared a great deal by the use of potassium iodide also was confusing. However, high voltage x-ray therapy was used over the hilus. Because of retention of secretion due to the neoplasm, the fungus probably had a good medium for growth. Whether the organism was a factor in the production of symptoms, and whether it aided in the destruction of tissue in the carcinomatous area is a matter for speculation. No bronchoscopy was performed, which would have assisted in an antemortem

diagnosis. The authors considered it advisable to have such a procedure performed, but their patient refused consent.

A case of *primary bronchiogenic carcinoma* in a boy, aged 10, is reported by L. K. Gould (J. Indiana M. A. 27: 332 (Aug.) 1934). An antecedent history of suspected aspiration of a piece of timothy grass confused the interpretation of the symptoms, particularly since they began immediately after the accident. Approximately 5 months from the day of onset, the boy suddenly died following a paroxysm of coughing. Two bronchoscopic examinations were performed during the course of disease, but no tissue was removed for fear of starting an uncontrollable hemorrhage. Postmortem revealed a Grade III carcinomatous involvement of the right lower lobe

F. C. Ormerod (J. Laryng and Otol. 48: 733 (Nov ) 1933) reviews a series of 27 cases of malignant disease of the bronchus, the large majority of which occurred in the male sex. The cases had diagnoses confirmed by biopsy. Several x-ray illustrations show that a growth in the bronchus is almost always convex, while a fusiform narrowing is probably due to chronic inflammation. According to F. L. Lederer (Arch. Phys. Therapy 15: 517 (Sept ), 608 (Oct ) 1934), physical signs are variable, but it is of interest to the laryngologist that a number of cases in his series presented themselves with laryngeal symptoms due to a paralysis of the recurrent laryngeal nerve. The bronchoscopic findings of compression or distortion, or of pulling over to one side of the trachea, indicated in these patients the possible presence of a tumor mass in the upper lobes, broadening of the carina and fixity of the tracheobronchial tree are pathognomonic signs.

Apparently no report in the literature of *primary melanoma of the bronchus* exists, according to L. H. Clerf (Ann. Otol., Rhinol., Laryng. 43: 887 (Sept ) 1934). He reports the case of a patient (female, aged 31) who developed a metastatic melanoma of the left main bronchus. One and one-half years previously, an irritated mole had been removed by fulguration and excision from the left arm. There was no recurrence visible externally. Deep radiation therapy did not inhibit the rapidity of the bronchial growth. Before death, 16 months after the diagnosis was made, a left-sided hemiplegia developed. Autopsy diagnosis: metastatic melanoma of the left main bronchus and trachea, with extension to the peribronchial lymph nodes, metastasis to brain, ovary, lung and skin.



# DERMATOLOGY

*by*

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**ACNE VULGARIS.**—*Prophylaxis.*—S. Nichols (J. Med. Soc. of New Jersey 31:556 (Oct.) 1934) believes that keeping the skin of the face dry and rather chapped prevents acne vulgaris during the period of adolescence.

He recommends the use of **soap** and **lotio alba** until the age of 15 is reached. To keep the skin dry, the face is washed before going to bed with castile soap and hot water; then well sopped for 5 minutes with lotio alba one-fourth strength. This treatment is continued until the skin is dry and chapped. The author has used this method of treatment in 47 children between the ages of 8 and 12. In 37 cases after from 3 months to 4 years of treatment the acne had disappeared.

**Treatment.**—In a splendid resumé of the subject D. J. Wilson (Nebraska State Med. J. 19:446 (Dec ) 1934) points out that treatment is naturally divided into 2 classes, *i e.*, the systemic and the local. He states further that the general physician cannot treat successfully the majority of acne cases unless he has the full cooperation of the patient. With juvenile cases, it is necessary to have the support of the parents.

Systemic treatment is as follows. The **diet** must be controlled, *i e.*, no pastry, candies, chocolate, sundaes, jams, jellies, preserves, pork or gravies are permitted. A minimum of white and rye bread, biscuits, potatoes, macaroni, cheese and nuts may be allowed. Alcohol is contraindicated. When the acne is under control, the diet may be more liberal.

*Constipation* must be corrected, and for this, usually 3 glasses of **water before breakfast**, going to the stool immediately after breakfast with the full determination to have **complete evacuation**, should be helpful. Occasionally, if the constipation is severe, some **laxative** in diminishing doses is necessary. Fluid extract of **cascara**, as a rule, works well and may be followed by diminishing doses of a **mineral oil-agar** preparation, preferably without phenolphthalein.

For patients who have a moderate *anemia*, **Fowler's solution** or the **cacodylates** may be prescribed. In severe cases, **liver extract** may be used.

Bromides and iodides should not be used and iodized salt is to be discontinued.

Although occasionally **vaccines** give good results, they are ordinarily unreliable.

Practically every patient with acne vulgaris also has dandruff. True dry seborrhea is a rarity. Unless the scalp condition is properly treated, the acne response will not be the best possible and not infrequently the acne returns after an apparent cure, if the scalp is neglected. When starting anti-seborrhea treatment the **scalp** should be thoroughly **washed** twice a week **with** a stimulating **tar soap**. After 2 or 3 washings, once a week will be sufficient. The hair should be brushed with a stiff bristle brush for at least 5 minutes each day. This mechanically removes some of the liquid sebum from the scalp and distributes it along the shaft of the hair, thus diminishing scaling. After the hair and scalp are thoroughly washed, a rinsing of hot water followed by cold is advised. A turkish towel with a moderate amount of massage may be used for drying and a good **hair tonic** used each day.

The following formula is very satisfactory :

<i>Hydrargyri chlor corros</i>	. . . . .	gr ij ( 0.2 Gm )
<i>Resorcin</i>	. . . . .	℥ ij ( 60.0 Gm )
<i>Acidi salicylici</i>	. . . . .	℥ ss ( 15.0 Gm )
<i>Glycerini</i>	. . . . .	℥ ss ( 15.0 c.c )
<i>Ol bay</i>	. . . . .	m iv ( 0.24 cc )
<i>Sp vini rectif</i> 70 per cent q.s.ad	. . . . .	℥ viij ( 240.0 c.c )

*Local Treatment.*—Many cases will respond to the briefly outlined general treatment given above.

**Ultraviolet irradiations** over the entire body, as well as locally, are valuable particularly in the young patients and especially if pus is present

Since all papules and pustules are secondary to the comedone, it is clear that if the **comedones** are all **removed** there will be no secondary lesions. Many dermatologists insist on doing this operation themselves; however, it is rare when some member of the family cannot be found who will do it just as well. Comedones, papules and small pustules can be taken care of in this way. Small lesions are often converted into large indurated ones if the work is too vigorously done and a comedone which is resistant to moderate pressure should be left alone after the first attempt for 2 or 3 days, when it usually responds to the second or third attack. Large pustules, nodules and cysts should be drained by the physician using a small sharp blade making a clean incision.

**Hot and cold packs** are valuable. They should be given as follows.

(a) A turkish towel is wrung from hot water and applied to the face for 2 to 5 minutes by the clock. The time depends upon the type of skin, the type of eruption and the physician's experience.

(b) The comedones are removed as previously directed.

(c) The débris remaining on the surface is removed when the face is thoroughly washed with soap and water and a rough cloth. At first a mild soap is used and as the skin becomes harder to chap, tincture of green soap and even surgeon's soap may be used.

(d) After drying, the entire face is gone over by squeezing it firmly between the thumb and forefinger. This squeezes onto the surface much liquid content of the sebaceous glands which prevents it from hardening and forming comedones.

(e) A fat solvent, such as carbon tetrachloride or equal parts of alcohol and ether, may now be sponged on the face, or soap and water may again be used and rinsed off with hot water.

(f) Cold packs are now applied for 2 or 3 minutes. Ice is not advisable.

(g) After drying, Dühring's lotio alba.

<i>Zinci sulphatis,</i>		
<i>Potassi sulphuret</i>	. . . . .	aa 5j ( 4.0 Gm )
<i>Glycerini</i>	. . . . .	℥ iss ( 6.0 Gm )
<i>Aque rosæ q.s. ad</i>	. . . . .	℥ iv ( 120.0 c.c )

is applied. If a stronger application is desired, Kummerfeld's lotion may be used.

<i>Sulphuris precipitati</i>	. . . . .	5j ( 4.0 Gm )
<i>Pulv camphoræ</i>	. . . . .	gr x ( 0.65 Gm )
<i>Pulv tragacanthæ</i>	.. .. .	gr xx ( 1.3 Gm )
<i>Liq calcis,</i>		
<i>Aq. rosæ</i>	.. .. .	aa f 5ij ( 60.0 c.c )



(h) If creams have been used previously as a "cleansing agent," the above schedule should be carried out only once a day at first and later increased to twice a day. Severe chapping is not desired and if such occurs, the applications are discontinued for a day or two. Pitting and scarring may be markedly diminished by exfoliating doses of **ultraviolet rays** following in as close succession as reactions will permit.

About 60 to 65 per cent. of average cases will be cured in from 6 to 24 months by the above method.

More poor results in the cure of acne are due to the failure to treat the concurrent seborrhea and a failure to remove the comedones than to any other cause.

*X-rays*.—Most general physicians are not equipped to give x-ray treatment. Although it is considered by far the most valuable single therapeutic agent available for the treatment of acne, it should be given by the specialist and does not fall within the domain of this paper (D. J. Wilson: Nebraska State Med. J. 19 446 (Dec.) 1934).

Many dermatologists have favorite combinations which from experience they have found to be of value. Darier prepared the following compound which is considered practical not only for the skin but for the scalp:

	Per Cent
<i>Powdered soap</i> . . . . .	40
<i>Lard</i> . . . . .	40
<i>Oil of almonds</i> . . . . .	20
<i>Essence of geranium</i> . . . . .	4 drops

He also used this soap mixture for the treatment of acne, but frequent complaints have been received that it separated, and that it was for the most part unpleasant to use. There is no question that the use of soap as a local agent is necessary in the treatment of acne; the disadvantage of most soaps is that they are so irritating when applied directly to the skin that they are frequently discarded by patients who should use them.

To overcome these disadvantages, in 1932 the following formula, based on the aforementioned compound, was prepared, the prescription has the advantages of the soap mixture but none of its irritating qualities.

	Per Cent.
<i>Stearic acid</i> . . . . .	20
<i>Liquid petrolatum</i> . . . . .	5
<i>Triethanolamine</i> . . . . .	5
<i>Cocoonut oil soap</i> . . . . .	40
<i>Distilled water</i> . . . . .	25
<i>Glycerin</i> . . . . .	5

It is made in the following manner:

Heat the stearic acid, liquid petrolatum and triethanolamine to 85° C. in a porcelain or glass container. Heat the distilled water and the glycerin to 85° C. in a separate porcelain or glass container. Maintain the heat at 85° C. and dissolve the cocoonut oil soap by agitation. Add the aqueous solution to the stearic acid mixture with slow but constant stirring. Remove the mixture from the source of heat and continue stirring until it is cool. Do not beat air into the cream.

The result is a smooth, pleasant mass which does not separate even in summer and which gives a good lather when mixed with water. J. G. Downing (Arch. Dermat. and Syph. 30:243 (Aug.) 1934) used it on sensitive skins and as an adjunct in the treatment of acne vulgaris and acne rosacea. It is applied with a pledget of cotton and removed with lukewarm water. The only disadvantage found is that up to the present time it is difficult in many places to obtain triethanolamine, but the resulting compound is not so good as the complete formula.

**DERMATITIS.—OCCUPATIONAL DERMATITIS.—In Coal Miners.**—G. B. Dowling and R. T. Brain (Brit. J. Dermat. 46:207 (May) 1934) discuss an epidemic causing papulopustular eruptions, which occurred recently among colliers working in a Kent coal mine. There were no constitutional symptoms. A man, who otherwise was in normal health, experienced an irritation while at work and developed a widespread eruption of more or less constant distribution within a few hours. This eruption became more widespread and more irritable during the succeeding few days whether the man remained at work or not and then if he ceased work, began to die down spontaneously. With one exception, in the case of those who remained at work no remission took place, and most of those who returned to work before the eruption had cleared up promptly relapsed. Some of those who recovered have since relapsed on returning to work. The eruption consisted of closely set punctate lesions involving in every case the extensor aspects of the thighs, knees, legs, buttocks and forearms and, in many cases, the flexural aspects of the forearms, the waist line, the chest and the back. In almost every case the eruption was most dense on the hairy part of the thighs, knees, buttocks and forearms. The lesions consisted of discrete papules, some were almost flat, many were scaly, and a certain proportion were capped by a small crust or pustule. In patients having rather dry skin the eruption consisted of flat, dry scaly spots of eczematous type, either discrete or aggregated into irregular patches. On the nonhairy parts of the skin, such as the abdomen, chest and back, the lesions were usually small dry papules, rather like those of the follicular variety of seborrheic eczema. A biopsy examined serially showed one of the lesions to consist of a superficial staphylococcal pustule with its sub-corneal colony of organisms. Direct smears and cultures from the pustules revealed the presence of *Staphylococcus albus* and occasionally *aureus*.

The etiologic problem appears to have 3 possible solutions. (1) The atmospheric conditions prevailing in the mine at the time were noxious to the miners' skins, perhaps because the mine was closed for a few days, (2) there was some new irritating property in the coal dust which, in combination with intense sweating, was capable of producing an irritant folliculitis, and (3) the condition might be due to infection in the mine with some fungus or organism.

**Of Milkers.**—Attention is called by N. Gottron (Med. Klin. 30:330 (Mar. 2) 1934), to "milkers' nodules," which were better known before the eradication of smallpox and are probably caused by a vaccine virus. From this type of nodules he differentiates telangiectatic granulomas, which are not pediculated on the fingers of milkers as they are in other persons. The absence of the pedicle may be due to the frequent compressions to which these formations are exposed.

on the hand of milkers. The author calls particular attention to nodular formations that are caused by the penetration of cow's hairs. These nodules vary in size between a grain of rice and a pea. They are bluish red and at the top may have a small scab or a necrotic layer. Occasionally hairs stick out from these nodules. Another disorder caused by the penetration of cow's hairs is a spindle-shaped thickening of the entire phalanx, and then there are the granulomas that develop in rhagades that have become irritated by the penetration of cow's hairs. The author describes the histologic aspects of the granulomas caused by cow's hairs, and he suggests that, in order to differentiate this type from milkers' nodules, the term milkers' granulation nodules should be applied to them. He considers **surgical measures** the best treatment for these nodules.

**DERMATITIS VENENATA.—Arsphenamine.**—TREATMENT.—Most cases of frank arsphenamine dermatitis present warning signs before generalized dermatitis begins, according to L. W. Shaffer (Arch. Dermat and Syph. 29: 173 (Feb.) 1934). If these warnings are sought, the dermatitis can probably be stopped before it gets a start.

Early prodromal cases offer a different problem than those showing frank exfoliative dermatitis. In most early cases treatment with arsphenamine may be guardedly continued by changing to a different type of arsenical, small doses, etc., until further sensitivity is determined. It is probable that a true allergic state does not develop in these early cases if treatment is stopped.

The addition of various substances to the arsphenamine to render it less toxic would be well suited to this type of case. Physiologic solution of sodium chloride, dextrose, gelatine, sodium thiosulphate and calcium have all been recommended for this purpose.

Another preventive measure of which there is little definite knowledge is **diet**. It has been shown that the presence of carbohydrates in rats materially increased the tolerance to arsphenamine, which observation required standardization of the diets of rats used in toxicologic tests on arsphenamine.

In some clinics the patients receive 2 or 3 tablespoonfuls of **dextrose** from  $\frac{1}{2}$  to 2 hours before treatment and it is thought to reduce reactions materially. **Sodium thiosulphate** has recently been the only popular detoxicating agent used as an adjuvant to the commonly employed methods of treatment. Clinical experience has proved that sodium thiosulphate is a valuable detoxicating agent for heavy metals, for arsenic in particular. Its value lies in its use early in the disease. After damage from arsenic has taken place, thiosulphate in any amount will fail to hasten the resolution of arsphenamine dermatitis. Sodium thiosulphate should, therefore, be given at the earliest possible moment. I would recommend that 1 Gm. (15 grams) of the freshly prepared solution be given intravenously at daily intervals for from 2 to 6 doses. A smaller dosage at the start is in line with the view that large doses would cause too rapid elimination, or freeing of arsenic from the tissues with subsequent exacerbation of symptoms. Sodium thiosulphate has a tendency to produce alkalosis, so that it should not be continued indefinitely.

Recent articles announce surprisingly good results in the *treatment* of post-arsphenamine dermatitis from injections of **liver extracts**.

Spiethoff states that the influence of treatment with liver in severe cases of arsphenamine dermatitis was soon apparent in definitely improved spirits, appetite, a decrease in temperature and in marked skin improvement. In experimental animals with severe intoxication from arsphenamine, with great emaciation and even prostration, great improvement followed injections of liver extract in from 1 to 2 hours. In man, he states, intramuscular injections of liver extract were painless and were given 3 times weekly in doses of from 5 to 10 c.c. ( $1\frac{1}{4}$  to  $2\frac{1}{2}$  drams). Liver extract may also be given by mouth.

Spiethoff states that in cases of mild dermatitis, treatment with arsphenamine could be continued in conjunction with liver extract without skin manifestations and that bismuth dermatitis is greatly improved.

The use of **calcium** in arsphenamine therapy goes back to B. Spiethoff and H. Wiesenack (Deutsche med. Wchnschr. 46 1219 (Oct. 28) 1920), who emphasized both the prophylactic and the therapeutic usefulness of calcium.

Gerwig recommended giving neoarsphenamine dissolved in 10 c.c. ( $2\frac{1}{2}$  drams) of a 10 per cent solution of **calcium gluconate** as a preventive of nitritoid crises, delayed fever, malaise. A conservation dosage calls for 10 c.c. ( $2\frac{1}{2}$  drams) of a 10 per cent solution of calcium gluconate intravenously and from 1 to 2 table-spoonfuls 3 times daily by mouth. Dosages in this amount are unknown in this country, which may explain the lack of success in its use in arsphenamine dermatitis.

The use of **dextrose** in solution of from 2 to 10 per cent. as a diluent for arsphenamine has been recommended by several investigators to prevent arsphenamine reactions, as well as its use by mouth preceding the injection. Arsenic combines with dextrose to form glucosides which are less toxic, which have a tendency to remain in the blood stream over a longer period, and which are excreted more rapidly.

The author proposes to treat any new patient of postarsphenamine dermatitis (nondiabetic) having accessible veins with 1 Gm. (15 grains) of **sodium thio-sulphate** and 50 c.c. ( $1\frac{2}{3}$  ounces) of a 50 per cent solution of dextrose injected intravenously daily for from 3 to 5 days. The administration of dextrose should be followed in  $\frac{1}{2}$  hour by 5 units of insulin.

Patients in whom venipuncture is difficult or impossible are to be treated with **liver extract** by intramuscular injection or with **calcium gluconate**.

In 2 cases of postarsphenamine exfoliative dermatitis observed by G. Zolezzi (Riforma Med. 50.609 (Apr. 21) 1934), in which a deficiency in the hepatic function was noted, they responded well to intramuscular injections of **liver extracts**.

**Ivy Poisoning** —PROPHYLAXIS—Observations in the prophylactic treatment of 14 cases of dermatitis venenata were made at the State Institute for the Feeble Minded at Letchworth Village, Thiells, N. Y. (Bull. of Lederle Laboratories, June, 1934).

Many of the inmates at this institution exhibit sensitiveness to *Rhus toxicodendron*. In fact, ivy poisoning occurs so frequently that the disease constitutes one of the chief medical problems of the institution during the summer season.

Fourteen patients who had experienced repeated and severe attacks in previous seasons were chosen. Each patient was given 0.5 c.c. (8 minims) of poison ivy extract in almond oil intramuscularly. Forty-eight hours after the inoculation the patients' arms were examined for evidence of local reactions. Five patients showed no local reaction of any sort, whereas the other 9 had areas of erythema varying in size from 1 to 4 inches. Of these 9 patients, 8 showed swelling and 6 developed a vesicopapular rash in the immediate vicinity of the inoculated area. Six days after the first injection 10 of the 14 patients received another 0.5 c.c. (8 minims) dose of the poison ivy extract intramuscularly. The other 4 patients, who had shown either no reaction or a slight one to the initial dose, received 1 c.c. (16 minims) each. The local reactions following the second dose in 48 hours were less pronounced. Again, 5 patients failed to react locally to the injected extract but 4 of these had given reactions to the initial dose.

Eight days after the second injection all 14 patients were given 1 c.c. (16 minims) each of the poison ivy extract intramuscularly. After 48 hours only 2 patients were completely free from signs of local reaction. The significant factor about the 14 patients comprising the study on poison ivy prophylaxis is that only 3 developed the disease during the following summer, despite the usual amount of exposure.

***Dermatitis due to Contact with Wood.***—A case of dermatitis, due to contact with wood, is reported by F. E. Senear (J. A. M. A. 101:1527 (Nov. 11) 1933) in which the face, neck, hands and forearms were affected. The clinical picture was obviously that of a dermatitis due to external irritation, so that a careful inquiry was made as to the causative factor. He volunteered the information that he had been scraping his archery bows just before the several attacks of dermatitis of which he complained. He had also on his own initiation applied some of the sawdust moistened with water to a relatively uninvolved area on the forearm, and when seen 24 hours later, showed a strongly positive reaction. This was repeated, the sawdust of white pine being used as a control. The latter gave a negative reaction, while the sawdust from the block of wood from which the bows had been made caused a definite positive reaction. The dust of the same two woods was soaked in alcohol and the tests repeated with the same result, except that the positive reaction was in this instance much stronger.

The best archery bows are made from the wood of the yew tree, and it was this wood imported from England, which had been used in this case.

Pusey reported a case of dermatitis occurring in a carpenter, which was found to be due to contact with sawdust of the common American poplar.

The importance of contact with woods and their dusts as a source of dermatitis is attested by the attention given to the subject by various officials in reports dealing with industrial hazards, probably the most important of which is the report on poisonous woods by the International Labor office at Geneva.

Among the woods which have received official attention from the industrial standpoint are coco-bolo, satinwood, teak, mohwah, lemon wood, acacia, Borneo rosewood, olive wood, cocos wood, sabicu and partridge wood. In several instances proximity to the tree alone is said to be sufficient for the production of a dermatitis.

The author's conclusions are as follows

Dermatitis due to contact with woods or their dusts is relatively common. Woods of tropical origin are most often incriminated, but it is probable that woods of temperate climates give rise to reactions more often than is generally supposed.

Eruptions may arise not only from direct contact, but also from proximity to certain trees and woods.

The majority of cases are seen in those whose occupation furnishes contact with woods or their dusts, and this furnishes an important industrial health problem well recognized by various official bodies

The toxic agents are most commonly nonsaturated resinous acids in a free state or alkaloids, but other types of chemical are responsible in some cases.

Development of dermatitis may ensue after contact of from a few days to several years, but in general the eruptions appear after a contact of from a few days to a few weeks

Freshly cut wood is, as a rule, most toxic, but in a few instances the wood becomes more toxic on seasoning

A variety of clinical pictures may result from contact with woods, but the usual reaction is an intense dermatitis venenata, often erysipelas-like, affecting the exposed parts

Perspiration and seborrhea increase the possibility of reaction

A number of symptoms due to involvement of other parts of the body, particularly the mucous membranes and the respiratory system, may occur

In the case of some woods, tolerance may be established, but, as a rule, sensitivity once established is persistent.

The cutaneous and general reactions may be regarded as an allergic reaction

**X-RAY DERMATITIS.**—*Treatment.*—M Craps and A Alechinsky (Scalpel, 87:497 (Apr. 14) 1934) advocate a simple technic consisting in **protecting the healthy tissues** with a screen of linen, pomade or tissue paper, and painting the lesion lightly with a 5 per cent aqueous solution of **silver nitrate**. In some cases to insure adherence to the solution and to facilitate its absorption, it is advantageous first to **wash** the affected area **with ether** and it is often necessary to clear the skin of squamas or less adherent crusts before application of the solution. The area is then exposed to a **quartz lamp** at an optimal distance of 20 cm. The period of irradiation varies from 5 to 10 minutes. In all cases it must be sufficient to produce complete drying of the solution and blackening of the area. If the color is not dark enough, the area is repainted until it becomes a glistening black. Since drying of the lesion begins from the time of the first application, the area treated should be covered only with a sterilized gauze compress. No fatty substances should be applied in the course of treatment. The patient is treated every other day. The authors studied 5 patients, all of whom responded well to treatment. Pains disappeared after 1 or 2 applications. Scar formation was rapid. The period of treatment in general was shorter than that required by any other method (maximum 10 months)

**DERMATOPHYTOSES**—*Pathogenesis*.—The conception of the “id” extended from the field of cutaneous tuberculosis by Jadassohn and Guth (Am. J. M. Sc. 187: 580 (Apr.) 1934) is one of the most important recent aspects of dermatomycology. In accordance with this conception, no inconsiderable part of the visible eruption of a dermatophytosis is a secondary sensitization phenomenon or dermatophytid in which no fungi are present—a dermatitis attributable to toxic or allergic reaction, from a primary focus sometimes distinguished with difficulty clinically from the general eczematous picture presented by the patient. A large proportion of the primary foci, or dermatophytoses proper, in which the fungi are present, are situated upon the feet, in the flexures of the groin, the anogenital cleft, and similar situations suitable for the growth of the fungus, while the secondary sensitization eczema and other “id” manifestations may be found upon the ears, the face, the palmar and dorsal surfaces of the hands, and in the form of more or less widely distributed dermatitic eruptions on the trunk and lower extremities. In addition to the eczematoid dermatophytids, an important and interesting group of “id” manifestations includes toxic erythemas, sometimes scarlatiniform, exfoliative and universal in distribution, erythema multiforme-like eruptions, presumably due to the distribution of the fungi *via* the blood stream and their fulminating destruction in the hyperallergic skin; and including even extensive bullous and hemorrhagic eruptions. The clinical pictures long classified as pompholyx of the hands and dyshidrosis, in which, according to the views of the German and Swiss school, the causative fungus is absent in the overwhelming proportion of cases, are dermatophytids.

It is important to realize that the secondary mycotic eruptions (“ids”) may not only give rise to confusing pictures of eczema, erythema multiforme, toxic erythema and exfoliative dermatitis, but that they may be accompanied by constitutional symptoms, most frequently observed in connection with the granulomatous mycosis called *kernion celsi*, a macaroon-like fungating tumor of the scalp, and including headaches, vomiting, anorexia, fever, marked regional adenopathy and leukocytosis.

**DERMATOSES**.—*Etiology*.—The cardinal eruptions caused by drugs ingested or injected are listed by F. Wise and B. Sulzberger (Pennsylvania M. J. 37: 973 (Sept.) 1934) as follows: (1) Truly eczematous eruptions with erythema, vesiculation, weeping and scaling are due to quinine, procaine hydrochloride, ephedrine, mercurials and sometimes arsphenamines. (2) Urticarial eruptions may be caused by belladonna, atropine, the morphine group and phenolphthalein. (3) Scaly erythematous eruptions, purely erythematous or scarlatiniform, and morbilliform and dermatitis exfoliative-like conditions are induced by arsenic, arsphenamine, belladonna, balsams and the heavy metals. (4) Phenolphthalein, antipyrine and salicylates produce erythema multiforme-like eruptions. (5) Erythema nodosum-like eruptions are due to iodides and bromides. (6) The effect of acneiform, furunculoid and erysipelas-like eruptions is due to bromides, iodides, chlorine, oils, tars, etc. (7) The causal drugs in ulcerating and vegetating eruptions are bromides and iodides. (8) Purpuric eruptions may be due to iodides, arsphenamines, particularly sulpharsphenamine,

and balsam (9) Phenolphthalein, antipyrine and sometimes the arsphenamines induce fixed and circumscribed, erythematous or bullous and polychromatic pigmented eruptions. Eruptions due to external medicaments and other irritants include almost all well-defined chemical substances, such as mercury, resorcin, butesin, butesin picrate, trinitrophenol, sulphur, chrysarobin, procaine hydrochloride, nupercaine, etc. There are many cases of eruptions in hypersensitive persons due to applications of medicinal salves, lotions, proprietary remedies and cases caused by skin contact during injection, but the overwhelming majority of the cases of eczematogenous substances can be eliminated and many cases of dermatitis avoided by the patch test. The patch test permits of the choice and employment of the least deleterious substances.

**Treatment.**—V Klingmüller (Med. Klin. 30:761 (June 8) 1934) noticed that painting with **chloroform** has a drying effect on the skin. In this respect it far surpasses benzine or ether. Moreover, it also has a certain bactericidal and fungicidal action. The author decided to try chloroform in various cutaneous disorders. In order to render the chloroform more stable, he added 1 per cent. of dehydrated alcohol, and, as the excretions of the skin generally have an alkaline reaction, he added a weak acid in the form of from 0.5 to 1 per cent. of cinnamic acid. Hoping that the drying effect of the remedy would inhibit the growth of cutaneous fungi, the author decided to try it in the various forms of mycosis of the skin. He obtained good results in  *pityriasis versicolor*, in  *erythrasma* and in the  *interdigital mycoses*. Many cases of suppurating cutaneous inflammations, such as  *acne* and  *folliculitis*, and many  *eczematous dermatitides* likewise responded to this treatment. Surprisingly favorable results were obtained in refractory cases of  *acne conglobata* and in papular forms of  *acne rosacea*. Later, the author tried the chloroform treatment even in chronic inflammatory changes of the skin, such as  *lupus erythematosus*, and he obtained some favorable effects. He believes that the treatment may be recommended in  *seborrhea* of the face and of the head. The  *juvenile hard warts* also frequently disappeared following painting with the chloroform preparation. An especial advantage of the preparation is that it does not cause discoloration. The chloroform evaporates shortly after the application, while the cinnamic acid remains in the form of crystals. The applications should be made from 3 to 6 times daily. The patient should be told to avoid inhalation of the chloroform.

M. S. Wien and M. O. Perlstein (Arch. Dermat. and Syph. 27:963 (June) 1933) report the use of **splenic extract** in 50 cases of  *itching dermatoses*, 25 of the group being afflicted with so-called eczema, and the second group of 25 cases included cases of seborrheic dermatitis, urticaria and dermatitis herpetiformis. The method utilized by the authors is the daily subcutaneous injection of 2 c.c. ( $\frac{1}{2}$  dram) of a 500 per cent. purified aqueous extract of hog spleen for 7 injections, followed by injections on alternate days during the second week and 2 or 3 times weekly during the third and fourth weeks, depending on clinical response. Pain at the site of injection is the most frequent reaction. Less commonly, general reaction was noted with fever, chill and general malaise appearing 12 to 18 hours after the injection and subsiding within 24 hours. Splenic extract in the authors' experience was of distinct value in  *urticaria*,  *dermatitis*



*herpetiformis* and *secondary toxic exfoliative dermatitis*. The clinical response varied from a complete cessation of itching with disappearance of lesions to only a diminution of pruritus. It has limited usefulness in the temporary alleviation of certain phases of eczema, tending to decrease pruritus and shorten the period of acuity. The results in a group of patients with the eczema-asthma-hay fever complex were unsatisfactory, the only benefit noted being temporary relief from itching. The authors are unable to support the enthusiastic claims made by a few observers, but believe splenic extract worthy of further investigation and a valuable method of trial in resistant dermatoses.

**ECZEMA.—Treatment.**—F. Gierthmuhlen (Munch. med Wchnschr 80: 1398 (Sept. 8) 1933) shows that the first three decades have brought great advance in the understanding of cutaneous disorders *in children*. The author differentiates dermatitis intertriginosa, dermatitis seborrhoides and crusta lactea from true eczema. The latter occurs primarily in children between the third and eighteenth months of life. Most investigators consider it an allergic phenomenon, more particularly a nutritive allergy, and in order to treat this form of allergy correctly, it is necessary to study the diet of the affected child for errors of a qualitative or a quantitative nature. It is essential to **avoid overfeeding**. In many instances it is possible to counteract the eczema by changing from whole milk to buttermilk or to skimmed lactic acid milk. The early addition of vegetables and fruit juices is advisable. If by changing from whole milk to buttermilk or skimmed milk the eczema does not disappear, other allergic factors, such as eggs, different types of flour or certain types of milk, must be searched for. It may, for instance, become necessary to replace cow's milk by goat's milk. Undernourished children with eczema have to be given adequate amounts of high-caloric foods. Eczemas in older children, which are frequently of a nervous origin, often yield to a vegetarian diet. However, nutritional therapy alone is not sufficient. The author considers ointments containing tar and powders helpful for local treatment. As especially effective he recommends a powder containing **sulphur and tar**. He found this preparation helpful in neurodermatitis of children of school age, but also in strophulus and in eczemas in which a pyogenic secondary infection has developed. In the latter conditions it is advisable to **soften the crusts** first by treating them **with oil**, and then to apply the **tar and sulphur powder**.

**BAKERS' ECZEMA.—Etiology.**—In examining 149 bakers suffering from eczema, O. Erna Zitzke (J Indust Hyg 16 201 (July) 1934) found that 41.8 per cent reacted positively to flours not treated with chemicals, but 67.2 per cent showed a positive reaction to flour to which chemicals (ammonium persulphate, acid calcium phosphate and potassium bromate) had been added. Of the 149 bakers, 86, or 58 per cent., reacted positively to the treated flour, whether the test was a subcutaneous one made with flour containing ammonium persulphate or a patch test with ammonium persulphate. Eight bakers alone reacted positively to ammonium persulphate patch tests, while the subcutaneous method of testing with treated flours gave negative results. The results indicate that the primary injurious substance in the treatment of flour is ammonium persul-

phate This leads in most cases to a hypersensitivity of the organism, which occurs only rarely in exposure to pure flour albumin. Whether it is the chemicals alone that produce the hypersensitivity or whether under the influence of these chemicals a molecular change takes place in the albumin which raises its allergic quality, cannot be proved by means of examination but can only remain in the sphere of probability.

**ERYSIPELAS.—Treatment.**—E. Neuber (Wien klin. Wchnschr 47:40 (Jan 12) 1934) employed **convalescent serum** in 36 cases of erysipelas and gained the impression that the defervescence and the disappearance of the toxic and of local symptoms are effected more rapidly and completely than was the case in patients who received nonspecific treatment. Only one of the 36 patients who received the specific treatment died, and this case had sepsis and phlegmon and was moribund when he arrived at the clinic. The author asserts that the administration of the convalescent serum produced no fever reaction; at least, the existing fever was not increased. The serum was administered by intragluteal and occasionally by subcutaneous injection. The usual dosage was from 20 to 40 c c, depending on age, weight and other factors. In the majority of cases 2 administrations were sufficient (from 50 to 80 c c), and in mild cases sometimes only 1 was required. The author believes that convalescent serum should have a leading place in the treatment of erysipelas. He ascribes the favorable results to the action of the specific protective substances that are present in the convalescent serum. Undesirable secondary manifestations, such as shock or delirium, were never observed.

**ROSENBACH'S DISEASE.**—This disease—erysipelas of swine—seems to occur in human beings more frequently than is generally supposed, according to W. Bachmann (Schweiz med. Wchnschr 64:38 (Jan 13) 1934). The diagnosis is easily made if the condition is borne in mind.

The cases reported by the author were those of butchers who contracted the disease in killing hogs. In the first case, the more severe one, the injection of **serum** was necessary in addition to local treatment with **ichthyol salve**. In the second case, local treatment alone resulted in cure. The erysipelas bacillus, normally an inhabitant of the intestinal tract of even healthy hogs, usually causes only local inflammation in man, but occasionally produces a general infection.

As a rule, the infection involves the fingers and edges of the hand.

In most cases local treatment is sufficient. Many physicians fear the severe general reaction following serum injections. The author sees no objection to the injection of serum in cases of progressive infection provided consideration is given to the danger of anaphylactic shock if tetanus injections have been given previously. The infection is an occupational disease.

**ERYTHEMA NODOSUM.—Etiology.**—From their observations based on 50 cases of erythema nodosum, L. Forman and G. P. B. Whitwell (Guy's Hosp. Rep. 84:213 (Apr) 1934) conclude that the condition is a reaction of bacterial allergy. They cite the following facts as suggesting that the tubercle bacillus is responsible:

1. Contact with open tuberculosis before the appearance of the nodes can sometimes be proved.
2. The appearance of the nodes is often preceded and followed by prolonged ill health.
3. In a certain number of cases frank tuberculosis develops subsequently.
4. Tuberculin tests are usually positive.

In the opinion of the authors, the theory that acute rheumatism or a streptococcal infection may cause the condition has not been proved. Pathological and bacteriological investigations of the nodes are likely to prove futile because the number of bacilli is small and bacteriolysis occurs quickly.

**Treatment.**—This should consist of **prolonged rest** until the nodes disappear, followed by further treatment with **fresh air, sunlight**, and more rest. In every case a search should be made for the probable tuberculous focus and for the probable social source of infection.

**FUNGOUS INFECTIONS.**—**Treatment.**—Y. Henderson (Arch. Dermat. and Syph 26:710 (Oct.) 1932) proposed the use of **formaldehyde vapor** for the sterilization and saturation of the leather of shoes and gloves. He states that when shoes have been so treated during the night, a distinct amelioration or disappearance of symptoms of *mycotic infection on the feet* is noted on the following day

C. W. Emmons (*Ibid.* 28:15 (July) 1933) found **iodine** and a surgical solution of **chlorinated soda** to have the highest phenol coefficient when tested against *trichophyton* and *monilia* suspensions.

B Levine (J A. M. A 101 2109 (Dec 20) 1933) used **phenyl mercuric nitrate** in *tinea* and *yeast infections of the skin* in 262 cases, of which 205 were cured. An ointment of equal parts of wool fat and an aqueous solution of the chemical in the strength of 1:125 or 1:150 by weight, with the addition of 10 per cent glycerin, applied twice daily, was found most satisfactory.

F. A. Taylor (J Am Pharm A 22 410 (May) 1933) found that the well-known effectiveness of **potassium permanganate solution** is probably due to the manganese rather than the permanganate element in the combination. **Manganous sulphate**, 1:100, in water, gave more striking results and 10 per cent **manganese oleate** in anhydrous lanolin was also effective in *foot infections*.

**FURUNCULOSIS OF FACE.**—**Treatment.**—S. Delling (Dissertation, Leipzig, 1933) states that during the nineteenth century it was generally believed that large and painful furuncles and most fluctuating furuncles of the face, as well as of other parts of the body, should be incised, whereas the smaller ones should be treated more conservatively, such as the application of clay and acetic acid compresses.

During the last decade, however, incision has been abandoned, especially in cases of furuncles of the face, and conservative treatment, as the passive hyperemia of Bier, the injection of autogenous blood, parenteral injections of protein, vaccine therapy, etc., has been employed.

Heidenhain and Fried, in 1924, recommended **x-ray** therapy for pyogenic infections of all types. In furuncle of the face 1 irradiation is usually sufficient

to cause central softening of the focus of infection and subsidence of the edema. The minimal superficial dose was 10 per cent. and the maximal dose was 25 per cent. of the skin erythema dose; 20 per cent. of the skin erythema dose is considered by most authors as the proper dosage.

Emmerich obtained healing of furuncles of the face in 3 or 4 days following irradiation with  $\frac{1}{10}$  of the skin-erythema dose with the use of a hard filter. A successful result consists of subsidence of the pains, improvement of the general condition, and absorption or accelerated resolution of the infection. Some authors believe early irradiation the most successful, whereas others (Schreuss) consider that the best results are obtained when the stage of ripening exists, usually about 8 days after the beginning of the infection.

Irradiation has no untoward effects and in a large number of cases the healing process is definitely accelerated. While recurrences were not prevented, their reabsorption was brought about quickly by early renewed x-ray therapy.

The mortality of furuncle of the face is still very high, according to Rodeliu, 87 per cent. Of 116 patients observed by P. Clairmont (Med. Welt 8:432 (Mar. 31) 1934), 43 per cent. died, all of a metastatic infection. A rapidly developing edema on the second to the sixth day with a temperature of over 30° C (86° F) is to be regarded as a sign of blood stream infection. An edema extending toward the middle angle of the eye is particularly dangerous because of the nearness of the angular vein.

The treatment must be conservative. In the cases reported, aspiration and incision were avoided, **talking and chewing food were forbidden. Linseed poultices or warm moist compresses were applied day and night.** Even when fluctuation appeared, no incision was done. **X-ray therapy and Bier's hyperemia** were used as adjuvants in selected cases.

The effects of the injection of autogenous blood and of the intravenous injection of antiseptics are of doubtful value.

For cases of *progressive thrombophlebitis* the author suggests **surgery**. This must be done before spread to the blood stream has occurred. Clairmont reports 2 cases of thrombophlebitis which were cured by strictly conservative treatment.

Surgical intervention is the preferable treatment in thrombophlebitis. The ligation of the venous path may be done in 3 sites: (1) beneath the medial angle of the eye, along the course of the angular vein, (2) above the clavicle, on the internal jugular vein along the posterior border of the sternocleidomastoid muscle, and (3) along the anterior facial vein in the submandibular region.

Clairmont believes that the future treatment of a furuncle of the face will consist in the local application of **warm moist compresses** and early proximal and distal **vein ligations**.

**HERPES ZOSTER.—Treatment.**—Three cases are presented by F. H. Gillett (Lancet 2:307 (Aug. 11) 1934) in which **solution of pituitary** was used for the treatment of herpes zoster. He has found that the injection of solution of pituitary is an uncertain and by no means an infallible treatment. It appears to act most dramatically when the *pain* is most intense. He offers no explanation of why this should be so, but the treatment is a valuable asset to the

practitioner in his attempt to relieve a patient from the intense pain accompanying herpes zoster.

**IMPETIGO.**—*Treatment.*—S. J. Levin (J. Michigan M. Soc. 33:533 (Oct.) 1934) used the following routine treatment for impetigo of the newborn in 44 consecutive cases. It has been successful in clearing up these cases in 72 hours or less, the average duration being 48 hours after the institution of therapy. All mature lesions were opened once or twice a day and the infant was immersed immediately for from 10 to 15 minutes in a bath of 1:15,000 **corrosive mercuric chloride** and a thorough soap bath was given with a mild castile soap. A **dusting powder** composed of equal parts of **bismuth subnitrate**, **light zinc oxide** and **mild mercurous chloride** was applied freely following the bath. New lesions were opened twice a day and the bath was repeated. After the first day only an occasional lesion appeared and only one bath was usually necessary. The bath should be continued for a few days after the last lesion appears. The dusting powder is applied freely during this period to the affected parts.

**KERATOSIS.**—*Arsenical Keratoses and Epitheliomata.*—The report of G. McNeer (Ann. Surg. 99:348 (Feb.) 1934), based on 3 cases of arsenical epithelioma and 1 case of arsenical keratosis, states that apparently the amount of arsenic taken is not of fundamental importance. In the cases observed the shortest period between the first ingestion of arsenic and the appearance of the cutaneous lesions was 1½ years; the longest, 17 years; and the average, 7½ years.

The lesions produced by arsenic are of 3 types, *i. e.*, dermatitis, keratoses, and epitheliomata. Acute arsenical dermatitis leaves a brownish pigmentation which may last for years. At first this is accompanied by scales, fissures, numbness, and tingling of the parts involved. The keratoses affect mainly the palms and soles, extensor surfaces, elbows, and knees. Arsenical epitheliomata are usually squamous-cell carcinomata of Grade 1 or 1 plus. They grow slowly and do not form metastases in the regional lymph glands until late. They are only moderately radiosensitive. The prognosis as to life is fairly good. A feature of the disease is the great multiplicity of the lesions that develop. As one group is cured, a new crop appears elsewhere.

The *treatment* depends on the form and extent of the lesions. In cases of dermatitis, the intravenous injection of **sodium thiosulphate** in amounts up to 1 gm. (15 grains) daily for 6 days has proved successful. In the cases reported by the author the best results were obtained by treatment with low voltage **x-rays** or a **mustard gas solution**. In the treatment of small lesions the **electric cautery** was found of great value. Surgical excision is rarely possible, as the lesions are too numerous. Application of **radium** plaques of 1000 mc hrs to each lesion has proved beneficial.

**LUPUS ERYTHEMATOSUS.**—In 47 cases of *disseminated* lupus erythematosus, G. A. O'Leary (Minnesota Med 17:617 (Nov.) 1934) found 26 showing clinical evidence of tuberculosis in one form or another. Tuberculosis was demonstrated in 5 of the 10 cases that came to necropsy. The principal

changes in the necropsy material were tuberculosis, endocarditis, infarcts in the spleen, diffuse nephritis and terminal bronchopneumonia. Pleural effusion and ascites from passive congestion were noted quite often. Anemia and leukopenia were present in half the cases. Cultures of the blood were positive in 4 attempts of 24 made in 14 cases. Of the 4 positive cultures, 2 were obtained from patients with endocarditis; the third was obtained while the patient was dying. Focal infection was noted in 40 cases. The 20 patients having the acute type died, on the average, 9 months following the dissemination of the disease, whereas 8 of the 27 patients with the subacute type died, on an average,  $4\frac{1}{2}$  years following dissemination. Seven patients with the subacute type are cured apparently. Treatment of the subacute type consisted of **rest in bed, transfusions of small amounts of blood, administration of quinine, plasmochin, small doses of gold sodium thiosulphate and x-ray irradiation** of the glandulous regions of the body. The evidence suggests that disseminated lupus erythematosus is a toxemia in which tuberculosis plays an insignificant part and that evidence of a specific infectious agent, although suggestive, is still lacking.

**Treatment.**—The method recommended by K. Steiner (Wien klin. Wchnschr 47:1019 (Aug 17) 1934) consists in the prolonged oral administration of arsenic in the form of solution of **potassium arsenite** mixed in equal parts with **tincture of ferrated extract of apples** and in a series of injections of an **oily emulsion of gold**. At first 3 drops of the mixed solution are given 3 times daily. This dose is increased daily or every second day by 1 drop until signs of arsenic irritation begin to appear (local inflammation and dissemination of small, new erythemas, eventually also cutaneous itching, dryness of the pharynx and burning of the eyes). The maximal dose should be from 15 to 20 drops 3 times daily. As soon as signs of irritation appear, the dose of the arsenic medication is rapidly decreased, but the arsenic medication should never be stopped suddenly, even if severe signs of irritation are present, for this would intensify the symptoms. At the time when the arsenic dose is rather high, at any rate when the patient is under a sufficient arsenic action, the intragluteal injection of the gold emulsion is begun. At first a 2 per cent oil suspension of **aurothiodextrose** is given in gradually increasing doses, and later increasing doses of a 20 per cent emulsion are administered. The highest single dose of the 20 per cent suspension of aurothiodextrose is 0.06 Gm (1 grain), and it is reached after from 12 to 15 injections. The highest doses (0.04, 0.05, 0.06 Gm— $\frac{2}{5}$ ,  $\frac{5}{10}$  to 1 grain) are repeated from 3 to 4 times. The intervals between injections are from 5 to 7 days. The total amount of gold suspension administered during the entire treatment is approximately 0.5 Gm ( $7\frac{1}{2}$  grains). The result of this procedure was that 14 to 19 patients with lupus erythematosus were cured in from 2 to 3 months. Nearly all of these patients had previously been unsuccessfully treated with other remedies. The cases with considerable dissemination seem to be especially suitable for this treatment. A complete explanation of the mode of action of the combined arsenic-gold therapy cannot be given as yet. However, the author assumes that arsenic changes the capillary walls to such an extent that the penetration of the gold salt into the tissues is promoted and the gold action thereby increased.

**LUPUS VULGARIS.—Treatment.**—H. T. Schreus and W. Engelhardt (Dermat. Wehnschr. 97:1595 (Nov. 11) 1933) report their experience with **borderline rays** in the treatment of patients with lupus vulgaris, most of whom were receiving the **salt-free diet** recommended by Sauerbruch, Herrmannsdorfer and Gerson. The irradiations were given with 9 kilovolts and 0.02 cm. of aluminum, which absorbs half the rays. The treatment was always local. The lupus was irradiated in such a manner that from 0.5 to 1 cm. of the surrounding normal skin was also exposed to the rays. The single dose never exceeded 1500 r. The dose should be large enough for a noticeable erythema and a slight swelling to become manifest in from 3 to 8 days. If the reaction does not develop until after this time, the dose was too small and a larger one has to be given the next time. The erythema persists from 1 to 3 weeks, and a new irradiation is not given until the erythema has disappeared, at the earliest after 10 days. In many cases an improvement may be noticed after the first erythema has disappeared; but in many others from 5000 to 6000 r., *i. e.*, from 3 to 4 irradiations, are necessary. The authors gained the impression that patients who received the salt-free diet reacted to the irradiations better and quicker than did those who were not subjected to this diet, but even when employed alone, the **borderline rays** may produce a cure. The irradiations with **borderline rays** are more effective than those with the quartz lamp, and yet the reactions are much milder. The treatment with **borderline rays** requires more time than, for instance, the treatment with the diathermy loop, but it has the advantage that it can be made ambulatory, as the reactions produced by the irradiations are not sufficiently severe to necessitate the cessation of employment. The authors warn against too early cessation of irradiations. They believe that many failures are due to the fact that the treatment is discontinued because the first irradiations do not seem sufficiently effective. The total dosage is, as a rule, from 6000 to 8000 r. The authors were able to produce a complete cure, even in a case of Boeck's sarcoid. Because of a comparatively small material, they are unable to give definite percentages of cures effected with **borderline rays** in lupus vulgaris, but they consider that a trial is always justified, for impairments were never observed.

W. Richter (Munchen med. Wehnschr. 81:644 (Apr. 27) 1934) combines the application of a **tuberculin ointment** with **quartz lamp irradiation**. In addition to concentrated tuberculin, the ointment contains killed but morphologically and chemically intact tubercle bacilli of the bovine and human types. To promote the antibody formation in the diseased area, quartz lamp irradiation was applied from a distance of 1 meter, beginning with a 5-minute exposure and gradually increasing by 1 minute each time. The surrounding areas were covered. It was assumed that the hyperemia and the resulting increase in the functional processes of the skin would increase the action of the tuberculin ointment. On the day following this treatment, a strong reaction with the signs of an acute inflammation was noted. As a rule, the treatment was repeated after 5 to 8 days. After 10 treatments a period of rest was given for from 4 to 6 weeks. If further treatment was necessary, a new series of treatments was started. Thus far, the author has employed the treatment only in patients with

extensive and severe lesions. In 2 cases the treatment was a complete success; not a single lupus nodule remained and the extensive lesions had healed with a flat, faintly red scar. In another case, considerable improvement was obtained. In 2 other patients only a few nodules remained after the treatment, and these were destroyed by means of **electrocoagulation**. Three other patients are still receiving treatment and in all the lesions show a tendency to heal. In 2 cases the treatment failed. The combined tuberculin and quartz lamp treatment was tried also in 3 cases of *erythema induratum Bazin* and cures resulted.

**MYCOSIS.**—In a large series of cases of mycotic infection of the feet D. Lieberthal and E. P. Lieberthal (Arch Dermat and Syph. 29 333 (Mar.) 1934) noticed that a moderate to advanced degree of flatfoot also was present. Of their 195 patients, 90 per cent had flatfoot and 30 per cent also had hyperhidrosis. The authors believe that, as a result of the changes of flatfoot, the resistance of the skin itself is lowered and the soil thus prepared for the invasion and subsequent growth of the fungi in epidermomycosis. Ten advanced and 5 moderately advanced cases of vesiculopustular lesions on the soles as well as intertriginous changes, accompanied by flatfoot, responded more rapidly to the ordinary forms of treatment after orthopedic correction. Not only did the lesions of the skin clear up rapidly, but the hyperhidrosis was also materially influenced. In 3 cases it disappeared completely. The rapid response of these resistant cases to the ordinary therapeutic measures following the correction of the foot deformity justifies the conclusion that **orthopedic corrective measures** are a therapeutic adjunct in the cases of fungous infection of the feet associated with flatfoot.

**PSORIASIS.**—*Pathogenesis and Treatment.*—O. Grutz (Deutsche med Wchnschr 60 1039 (July 13) 1934) recapitulates his studies on psoriasis in which he proved that psoriasis is caused by a disturbance in the fat metabolism and that it can be counteracted by a diet deficient in fat. He gives instructions about the foods that should be avoided. He stresses particularly all types of fats (bacon, lard, butter, cream, oil, etc.), meats with a high fat content (pork, mutton, goose, duck, etc.), certain fish (eel, herring, salmon, carp and all fish roe) and egg yolks, the latter on account of their cholesterol content. Cakes and other baked foods containing fats must likewise be avoided. Permitted are lean meats, fish with a low fat content, soups, and vegetables, provided they have been prepared without fat, fruits and berries, preserves and fruit juices and various breads that have been prepared without fat. On such a diet, obese patients with psoriasis frequently lose weight, while patients of normal weight do not, provided their calory requirements are adequately supplied in the form of carbohydrates and proteins. Emaciated persons with psoriasis have even been known to gain in weight under the influence of the fat deficient diet. The author discusses the possibility that just as the carbohydrate tolerance differs in diabetic patients, there may be a difference in the fat tolerance of psoriatic patients. On the basis of clinical manifestations this seems probable, for in some patients a slight reduction in the fat intake is effective, while in others a more strict regimen is necessary. Moreover, it is advisable to investigate whether the



fat synthesis is disturbed in psoriatic patients. The author reports that in some patients the results of the fat-deficient diet are already noticeable after 2 or 3 weeks, while in others 6 weeks or even several months are necessary to reveal the effects. In some patients the psoriatic lesions spread in area but decrease in depth shortly after the onset of the treatment, and there may also be a temporary increase in scaling; this should not, however, tempt the physician to interrupt the treatment, for this "becoming acute" is only temporary and the continuation of the diet will finally effect the complete disappearance of the lesions.

Reports of favorable effects of **liver therapy** in psoriasis induced T. Gruneberg (Dermat. Wchnschr. 97:1793 (Dec. 23) 1933) to try this treatment. Injections of liver extract were given every second day, and the patients took liver by mouth in the form either of fresh liver or of liver extract. In psoriatic patients, liver therapy decreases the tendency to relapse; but it also influences the existing cutaneous manifestations. It appears that the therapeutic effect is better if the patient is exposed to the influence of light, but the exposure should not be too severe. In order to compensate for the deficiency of sunlight in the big city, particularly during the winter months, the patients were given **quartz lamp irradiations**; but the doses were smaller than is usually the case, in order to avoid irritation. In spite of the fact that the liver therapy occasionally produces surprisingly good results, the author admits that, aside from a reduction in the tendency to relapse, it accomplishes, on the whole, no more than the usual methods of treatments; for liver therapy may fail as well as the other treatments, and, as a rule, it does not make the application of ointments unnecessary. The mechanism of liver action, which may involve several components, is not yet clear, but it is possible that an increase in the sulphur or glutathione content of the skin is an essential factor.

T. Gruneberg (Klin. Wchnschr. 12:1908 (Dec. 9) 1933) has been able to show that when psoriatic efflorescences tend to disappear, there is an increase in the sulphur content of the skin. Since the suprarenals, particularly their cortex, are the most important organ in the regulation of sulphur metabolism, he decided to determine in what manner psoriatic changes in the skin react to treatment with an extract of the suprarenal cortex. Other investigators, particularly Hauck, had tried medication with epinephrine in drops or in the form of tablets, but had obtained no results. The author used an **extract of the suprarenal cortex**, 1 c.c. (16 minims) of which corresponded to 50 Gm. (1 $\frac{1}{2}$  ounces) of fresh substance, but the epinephrine content was not in excess of from 1 to 2 micrograms. The patients were given daily intragluteal injections of from 2 to 3 c.c. (32 to 48 minims) of the extract. In all cases, generally a few days after the beginning of the treatment, the psoriatic lesions showed signs of retrogression. Only the cases of psoriasis punctata were more resistant and did not react until from 2 to 3 weeks after the injections had been begun. An insufficient supply of the extract necessitated interruptions in the treatment of several patients, but the author nevertheless gained the impression that the extract of the suprarenal cortex is more effective in the treatment of psoriatic exanthems than are the liver extracts that have been used in recent years. In a patient

presenting polyarthrititis, it was noted that the pains disappeared and that the mobility of the joints improved under the influence of the suprarenal extract. Another observation that the author considers worthy of note is the fact that in 5 of the 12 patients who were treated with the extract, the healing of the psoriatic lesions was accompanied by depigmentation. Although this phenomenon was generally only temporary and although leukoderma psoriaticum is not as rare as is commonly assumed, the increased incidence is nevertheless significant. The author considers it an interesting contribution to the hormonal modification of cutaneous pigmentation, particularly in view of the pigmentation in Addison's disease.

**TATTOOING.**—*Method of Removal.*—A freshly prepared ointment is used by H. Stroth (Munchen. med. Wchnschr. 81.753 (May 18) 1934) consisting of 7 Gm. ( $1\frac{3}{4}$  drams) each of **pyrogallic acid**, **salicylic acid** and **resorcinol**; 5 Gm. ( $1\frac{1}{4}$  drams) each of **glycerin** and **dilute alcohol**; and 1 Gm. (15 grains) of **tragacanth**. The area around the tattooed pattern is protected by covering it thickly with **zinc ointment**. A piece of impregnated gauze, the size of the tattooed area, is covered with the caustic ointment and is applied to the tattoo in such a manner that the margin of the gauze rests on the zinc paste. The entire application is securely fixed by layers of gauze and by adhesive tape. This bandage is removed after 24 hours. At this time the epidermis can be removed. A new caustic ointment bandage is applied in the same manner as the first, but this second one is left in place for 48 hours. After this time the area has usually become necrotic, and only in exceptional cases does a third application of the caustic ointment become necessary. As a rule, the area may be cleansed with oil after the second application, and then the necrotic tissues gradually slough, the process being completed in from 5 to 7 days. Following that, granulation sets in and in the course of 3 or 4 weeks a smooth scar has taken the place of the tattoo.

**VERRUCA.** — *Treatment.* — An aqueous 1.5 per cent solution of **bismuth sodium tartrate** was employed by H. Shellow (Illinois M. J. 66 301 (Oct.) 1934) in the treatment of 97 lesions of various types of verruca occurring in 73 patients. The skin about the lesion is prepared by washing with soap and water, iodine and alcohol are then applied. A fine hypodermic needle is used to pierce the skin just outside the zone of hyperkeratosis and directed downward and inward toward the base of the verruca at the most active point, the end of the needle remaining just above the corium. From  $\frac{1}{2}$  to 2 minims (0.03 to 0.12 c.c.) of the bismuth sodium tartrate solution is injected, according to the size of the lesion. In from 1 to 3 days after the injection a dark hemorrhagic area appears, visible through the keratotic surface. This denotes that the drug has taken effect. In the markedly keratotic hard type of ordinary verruca vulgaris, this phenomenon may not always be seen. In most cases, from 1 to 3 days after the first injection there has been either a complete cessation or a marked diminution of pain. The peripheral redness that so often accompanies the painful verruca disappears in from 2 to 7 days. All papillomatous lesions flatten out decidedly after the first injection, and in the plantar or palmar types the surface

becomes smoother. If within 7 to 14 days following the appearance of the hemorrhagic center the top of the verruca has not come off or the central portion has not fallen out, the keratotic tissue may be removed to determine whether any activity is still present. In most instances, after a lapse of from 14 to 17 days following the initial injection, the removal of this hemorrhagic keratotic center reveals an underlying normal appearing epidermis. If after 2 weeks of further observation an active verrucous tissue is seen, the lesion may be reinjected. Of the 97 lesions, most of them having been treated previously by other measures, 89 were cured, 5 improved, and 3 showed no improvement. Sixty-seven lesions were of the painful palmar or plantar variety, and 18 were of the verruca vulgaris type occurring on the dorsum of the hands or feet.

**VITILIGO.—Treatment.**—In a case of leukoderma, M. H. Cohen (Arch Dermat. and Syph 28:215 (Aug.) 1933) instructed the patient to apply a 10 per cent. **alcoholic solution of oil of bergamot** to all the affected areas twice a day. **Ultraviolet irradiation** with the carbon arc lamp was applied to the face for from 3 to 5 minutes twice a week, and an intravenous injection of **gold sodium thiosulphate** (0.1 Gm.— $1\frac{1}{2}$  grains) was given once a week. Within 2 weeks the areas on the face had begun to coalesce. At each visit the hyperpigmented patches were seen encroaching on the depigmented spots, and in 6 weeks the face was completely free from any evidence of the disease. The patches on the thighs and abdomen were also lessened, but the improvement was not as rapid as it was on the face, which had received ultraviolet irradiation in addition to the oil of bergamot. The patient was treated for 14 weeks, during which period she received a total of 1.4 Gm. (22 grains) of gold sodium thiosulphate. The other vitiliginous areas were treated by several ultraviolet irradiations, with excellent results. She was seen 1 year after the last treatment, the vitiliginous areas had not returned. Her face was completely free from any pigimentary disfigurement, and the patches on the thighs and abdomen were greatly improved.

**XANTHOMATOSIS.—Treatment.**—The **x-ray** treatment in a case of xanthomatosis is described by J. Frimann-Dahl and R. Forsberg (Acta radiol. 14:506, 1933). This treatment was applied to the different foci and had a striking effect. X-ray pictures showed a gradual diminution of the xanthomatous areas and a corresponding regeneration of bone substance.

Parallel with the favorable effect on the local processes, there was a striking improvement in the secondary symptoms and in the general condition. The symptoms of intracranial pressure disappeared, the growth of the patient increased, and the blood cholesterol was reduced to normal. After 2 years the patient was practically free from symptoms.



# RADIOLOGY

*by*

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**X-RAY DIAGNOSIS.—Appendicitis.**—In discussing the x-ray diagnosis of appendicitis, T. Scholz (Am. J. Roentgenol. 31:792 (June) 1934) believes that tenderness over the appendix elicited during the *fluoroscopic examination* is the only sign of proven value. Failure to obtain this sign does not exclude an appendiceal lesion, but does indicate that no active inflammatory process is present at the time of the examination. An x-ray study of the appendix is useful chiefly in differential diagnosis. It should always embrace the stomach and small and large bowels and may also include the urinary tract and lower spine as well as the lungs and pleura. It is worthy of note that gross anatomical changes may be found in appendices that have been clinically normal; hence, such changes do not furnish proof of chronic appendicitis. The therapeutic result affords a superior criterion.

**Colon, Cancer of.**—H. Shay and J. Gershon-Cohen (Surg. Gynec. Obst. 58 52 (Jan) 1934) advocate the use of the **double contrast enema** in the study of the colon, particularly in cases where early *neoplastic lesions* are suspected. Their technic consists of the administration of the ordinary barium enema (8 ounces—240 Gm.—of barium sulphate to 2 quarts—2000 c.c.—of water), which is studied by the usual fluoroscopic and radiographic methods, and the further study of the colon after the patient has voluntarily emptied it and the bowel has been moderately distended with air introduced by a small Politzer bag and rubber tube.

The normal colon retains about 25 per cent of the barium enema after evacuation and this residue forms a sharp, uniform, etched colonic outline against the subsequently introduced air. This method of examining the colon is particularly helpful when searching for *small neoplasms, intraluminal polypi, diverticula* and *ileocecal tuberculosis*.

**Colon, Diverticula of.**—R. Golden (New England J. Med. 211 614 (Oct 4) 1934) discusses the x-ray diagnosis of diverticulosis of the colon and states that in the great majority of cases an x-ray examination will easily demonstrate the condition. A **barium enema** or barium meal is administered so as to fill the sacculations with the contrast medium. These then appear as bud-like projections from the contour of the intestinal wall. The enema is preferable to the barium meal by mouth in all cases where a partial intestinal obstruction might thereby be made complete. The *differential diagnosis* between *diverticulitis* and *colonic carcinoma* is a difficult one to make, but the following findings are extremely helpful. In cancer of the colon there is destruction of the mucosa in the affected area so that the normal folds are not demonstrable, while in diverticulitis these folds are usually exaggerated. In carcinoma, the constriction, when present, is permanent with respect to its size and shape, while an inflammatory constriction is variable in width, and the details of mucosal contour are subject to change. Golden finds that the association of colonic cancer with diverticulosis is infrequent and that when the two conditions appear in the same patient, the neoplasm may occur in a portion of the bowel that is free from diverticula. He summarizes his radiologic experiences with these diseases of the colon as fol-

lows: Diverticula of the colon may give rise to symptoms on the right as well as on the left side of the abdomen

In spite of the fact that the difficulty in differentiating diverticulitis and carcinoma has long been known and in spite of the development of roentgen methods of examination, errors in diagnoses are still made. Some of the errors from the roentgenological standpoint seem to be due to a failure to realize that diverticula do not always fill, following a barium enema, and to appreciate the significance of the intestinal wall contours. The deep, exaggerated mucosal folds raised up by an infection produce a barium shadow with irregular, jagged, saw-tooth margins. The infiltrating growth of an annular carcinoma, on the other hand, destroys the mucosa and produces a constriction with relatively smooth margins in which no mucosal contours can be seen. Either condition may cause a complete obstruction to the flow of the barium enema, in which case no differential diagnosis can be made. An infectious granuloma which destroys the mucosa cannot be differentiated by roentgen methods from carcinoma

The incidence of the association of diverticulosis with carcinoma of the colon is very low. There is no convincing evidence that the former predisposes to the latter

Because his method gives information concerning the inside of the gut, the roentgenologist has a much better opportunity to differentiate inflammation and malignant disease of the colon than the surgeon who, even at operation, can only palpate the outside of a hard mass. Although this differential diagnosis roentgenologically may be difficult in individual instances, with consideration of the above mentioned points it should be accurate in a high percentage of cases

**Diaphragmatic Hernia.**—The infrequency with which diaphragmatic hernia is diagnosed clinically is noted by L. B. Morrison, S. L. Morrison and J. H. Delaney (New England J. Med. 210: 624 (Mar. 22) 1934) and the necessity of a painstaking radiologic investigation when this condition is suspected is emphasized. The symptoms are surprisingly variable and the complaints of the patient depend to a large extent upon the organs involved in the hernia. The symptomatology may, therefore, be abdominal or thoracic, or both. The *most common abdominal symptom* is vague pain or distress just under the xyphoid during or after meals, the *most common thoracic*, a feeling of fullness in the chest after eating or upon retiring

The x-ray diagnostic technic consists of careful fluoroscopic examination of the esophagus and stomach following preliminary films of the thorax in varying positions with the patient erect. Morrison and his associates call particular attention to the value of fluoroscopy in detecting the presence of diaphragmatic hernia, the patient being screened from all angles and in all positions from erect to Trendelenburg

**Dyschondroplasia.**—The x-ray diagnosis of this condition is described by A. Bonola (Chir. d. org. di movimento 19: 101, 1934), who states that, as a general rule, all the *metaphyses* and *epiphyses* of one side of the body show involvement from the beginning. The x-ray appearance is most characteristic in the case of the more rapidly growing metaphyses, *i. e.*, the distal one at the elbow and the proximal one at the knee, and indicates an abnormal and atypical pro-



liferation of cartilage in bone. Inasmuch as subjective symptoms may be entirely absent in the early stages and since the disease simulates rickets, x-ray examination of the entire skeletal system should be carried out. Unfortunately, no medical cure of dyschondroplasia is known.



Fig 1—(A) Cecum and ascending colon, immediately following evacuation of barium enema, on seventh day of illness. Note residue in cecum. Appendix is long and its distal half irregularly dilated.

(B) Same case. Cecum and ascending colon about 75 days after treatment began. Note small filling defect along medial aspect of cecum near base of appendix, which is no longer dilated as in Fig. A.

(C) Shortening of ascending colon and slight irregularity and induration of cecum.

(D) Same colon as seen in Fig. C, 12 days later after a course of treatment. (K. Ikeda, Radiology.)

**Dysentery, Amebic.**—K. Ikeda (Radiology 22: 610 (May) 1934) records his experiences in studying by x-rays the colons of 7 persons that had contracted amebic dysentery during the summer of 1933. The x-ray appearance of the bowel varies according to the stage of the disease. In the earliest stages no detectable changes are observed, somewhat later, multiple projections on the colonic contour appear, probably representing superficial ulcerations. When the

lesions involve the submucosa and muscularis, fine "feathery or thorny" filling defects are observed in the barium shadow. When the patient is in the subacute or early chronic stage, the cecum and ascending colon appear shortened and contracted, giving a rather characteristic deformity. Following the exhibition of emetin, these changes disappear. X-ray studies of the colon in amebic dysentery are obviously of more value in guiding the treatment than in making a diagnosis.

**Encephalography.**—A. Radovici and O. Meller (*Presse méd.* 42:153 (Jan 27) 1934) report their experiences with the use of **thorotrast** as a medium in encephalography. Following exhaustive tests upon animals, they concluded that the safety of this substance permitted its use within the meningeal spaces of human beings. Their technic comprises removal of 10 c.c. of cerebrospinal fluid through a **cisternal puncture** and its replacement with 10 c.c. of thorotrast. Following this injection, the patient is maintained in a head-down position for 15 minutes, to enable the contrast substance to diffuse over the hemispheres as well as to permeate the ventricular system. When the x-ray films have been exposed, **lumbar puncture** is performed in an attempt to drain out as much of the thorotrast as possible, with, however, but indifferent success. All patients show a pronounced meningeal reaction the next day and have headache, vomiting and fever. Ultimately, these symptoms disappear and no permanent ill-effects are noted. Radovici and Meller feel that future chemical refinements will render this medium more suitable for encephalography.

**Fetus, Radiography of.**—W. O. Weiskotten (*Radiology* 20:58 (Jan) 1933) reports his experience with the radiologic diagnosis of *anencephaly* prior to delivery of the child. A history of hydramnios, convulsive movements of the fetus, and inability of the obstetrician to locate accurately the fetal head, suggests the possibility of this condition and calls for a radiographic study of the case. A typical x-ray picture clearly demonstrates the cranial malformation and indicates to the obstetrician the problem that confronts him.

**Heart, Kymography of.**—An editorial in the *British Journal of Roentgenology* (*Ibid* 7:705 (Dec) 1934) calls attention to the development of x-ray kymography of the living heart as a procedure of great diagnostic value, particularly when dealing with proved or suspected cases of **myocardial degeneration**, where the electrocardiographic report is so often negative. Kymography now rests upon a sound basis and with a standardized technic should prove invaluable in cardiac diagnosis. In this connection, the work of I. S. Hirsch (*Ibid* p. 728) is of particular interest. His apparatus comprises the usual x-ray machine, a sheet of metal with regularly spaced narrow slits which is placed in front of the thorax of the patient, and an x-ray film in front of the metallic sheet, this film being capable of a definite amount of movement, at a specified rate, at right angles to the direction of the slits. With the apparatus in operation, therefore, the movements of the cardiac contour are projected through the slits upon the moving film as series of waves, and a subsequent analysis of the individual waves (corresponding to the respective portions of the cardiac contour) reveals the departures from normal form and altitude that indicate the presence and the nature of the underlying pathological condition.

"Deviations of the kymographic appearance from the normal may result from:

"1. *Disturbances of rhythm* which produce variations in the character and periodicity of the movements.

"*Cardiac Irregularities.*—By a study of successive cycles, the presence of disturbance in rhythm may be demonstrated by noting the variations in the

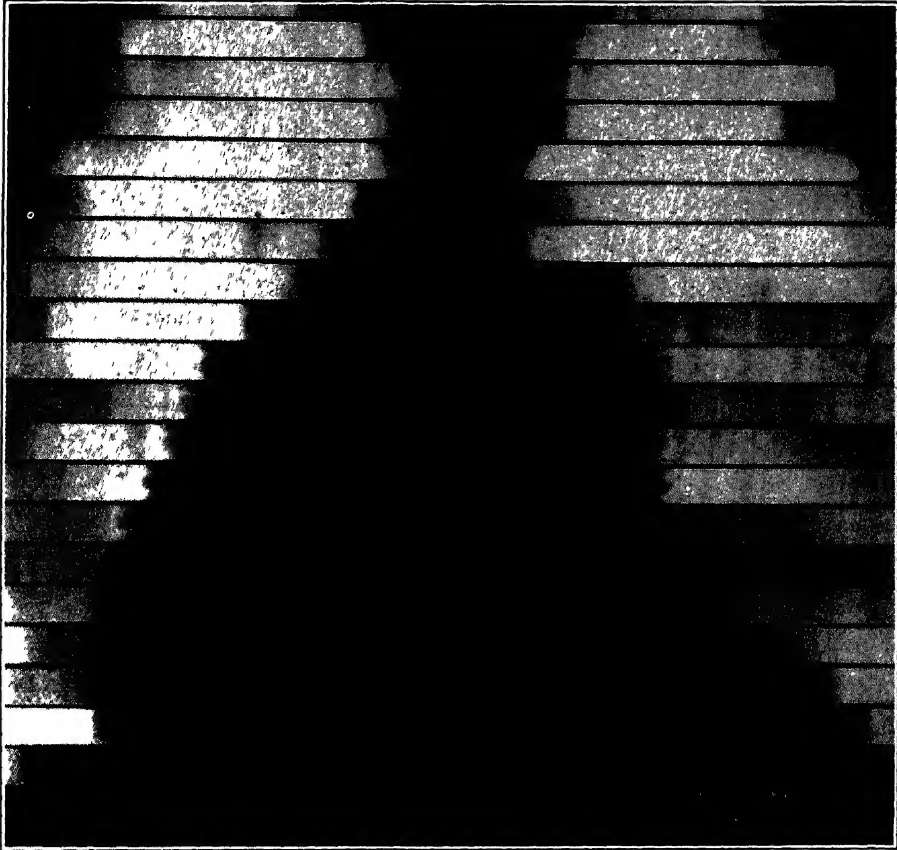


Fig 2—Kymogram of case of mitral stenosis and insufficiency Characteristic contour may be made out Note inconspicuous aortic waves and prominent pulmonic and auricular waves Ventricular waves are also prominent over almost entire right cardiac contour. Diastolic limb of ventricular waves is a straight line without the usual break. Then follows a plateau indicating absence of movement of left ventricle, to be followed by a rapid systole. (I S Hirsch Brit J Radiol)

amplitude and time relationships of the waves Arrhythmias, extrasystoles, auricular fibrillation and flutter, and heart block may thus be graphically demonstrated

"2 *Intrinsic changes* in the musculature, hypertrophy, atony or degeneration

"*Degenerative changes* in the heart or vessel wall resulting in sclerosis, calcification or aneurismal dilations modify the character of the waves to a varying degree.

"Partial *aneurism* of the heart may be shown kymographically by waves of diminished amplitude over a localized area of ventricular contour with normal waves above and below the area. When an actual sac is present there is a definite

reversal of the waves over a localized area. With each systole the inward moving limb is replaced by an outward diastolic movement, because the walls of the sac, having lost its contractility, become distended by the systolic pressure in the ventricle. In other words, there is present in the ventricular contour a wave having the time and form characteristics of the aortic wave. The amplitude of the wave is diminished over areas of the heart, the seat of extensive hypertrophy.

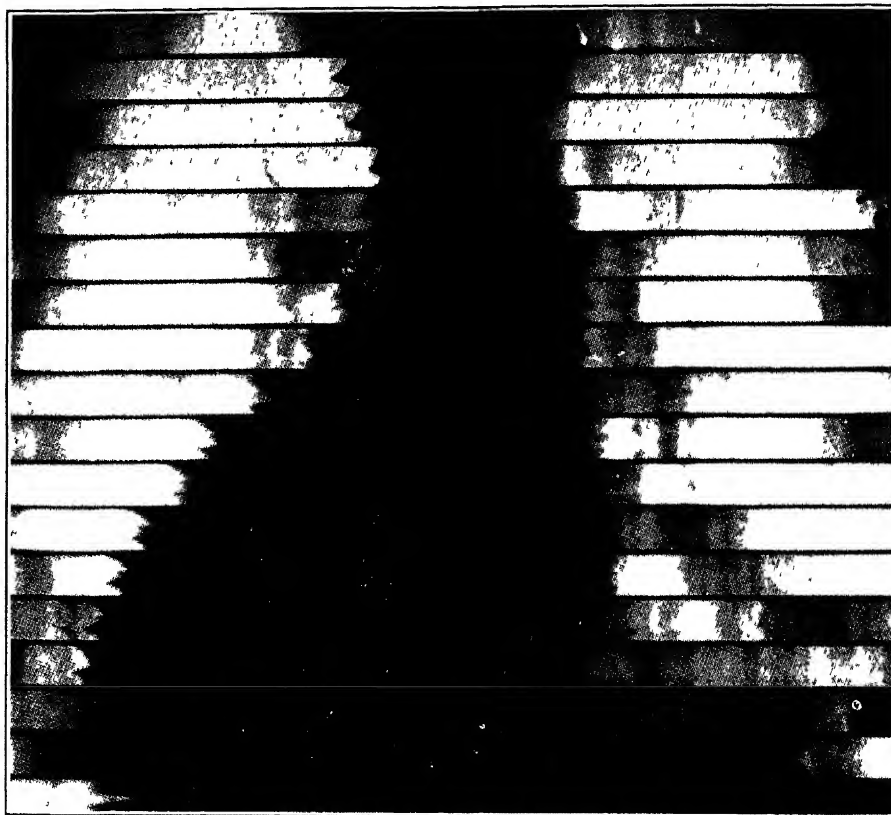


Fig. 3—Kymogram of the heart of aortic insufficiency. Normally, there is a difference of about  $\frac{1}{100}$  of a second between beginning of systole and peak of aortic wave on the ascending arch and this particularly coincides with peak of aortic wave on the descending arch (less than  $\frac{1}{100}$  of a second). In insufficiency of aortic valve, peak on the ascending arch is attained almost simultaneously with closure of mitral (about  $\frac{1}{100}$  later), but peak on the descending arch is not attained until about  $\frac{6}{100}$  of a second. Failure of aortic valves to close produces dilatation of the ascending arch immediately, but delay to the descending arch is compensatory in order to establish necessary ventricular aortic pressure. On the ascending arch, aortic wave rises rapidly, falls back slowly at first and then drops suddenly and sharply. On the descending arch, wave rises rapidly, falls back sharply and then retracts slowly. The left auricular waves are exceedingly prominent. Vibration associated with second sound shows in an exaggerated form over ventricles, but first sound vibration cannot be made out. (I. S. Hirsch Brit J Radiol.)

“The waves over aortic aneurismal dilatations vary in size. Waves of high amplitude or none at all may be found, depending on the extent of thromboses. Aneurisms of the ascending aorta usually show very pronounced waves. The form of the wave may be symmetrical. However, in other cases the characteristics of the aortic wave may not be changed over the aneurismal area, though a slight delay in point of time may be found on comparing the peak of the outward thrust to that of a normal portion of the aorta.

"*Sclerotic changes in the aorta* do not change the character of the aortic wave, except when associated with hypertension, when the amplitude of the aortic wave is small and the apex is blunted. The associated ventricular hypertrophy may be responsible for the waves of increased amplitude, which may not be influenced even by extensive calcification.

"3. Changes resulting from *valvular defects* which produce abnormal vibrations and variations in the chamber movements.

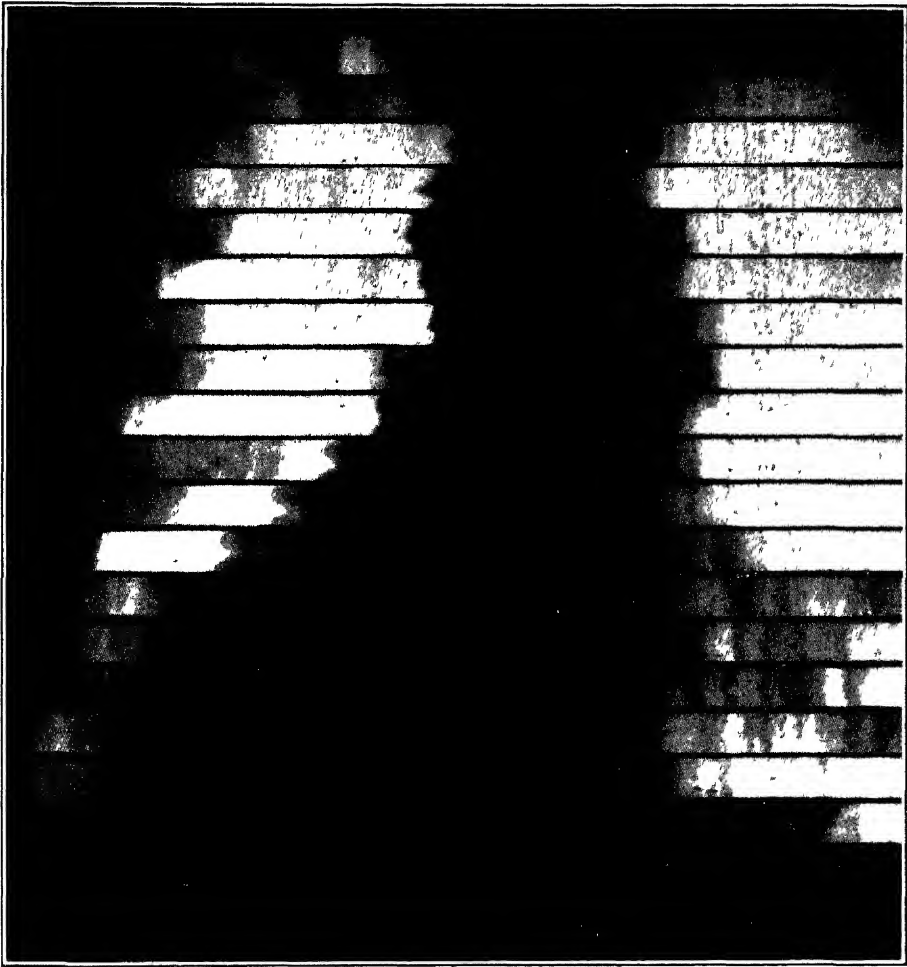


Fig. 4—Kymogram of case of aortic stenosis with marked left ventricular enlargement. Over lower part of left ventricular contour are waves which have the shape of aortic waves. Peaks of these waves correspond almost exactly to the ventricular systole. (i.e., this small portion of the heart contour moves outward when remaining portions of ventricle move inward. This would indicate an area of myocardial degeneration and a ventricular aneurism. (L. S. Hirsch—Brit. J. Radiol.)

"Among the primary results of valvular disease are

"(a) A variation from the normal state of filling of the chambers related to the valve involved

"(b) Secondary and compensatory changes in the muscle walls

"These changes produce.

"(a) Modifications in the normal distribution of the waves

"(b) Modifications of the normal characteristics of the waves.

"4. Extracardiac influences which modify the anatomic relationship of the heart and the intrathoracic pressure changes."

**Lung, Cancer of.**—It is estimated by E. A. Graham (Am. J. Roentgenol. 31:145 (Feb.) 1934) that primary carcinomata of the lung comprise between 5 and 10 per cent. of all of this type of malignancy. Prominent among the clinical features are the insidious onset and the persistent productive cough with pain in the chest in a man past middle age. If the sputum is blood-streaked and a pulmonary lobe is found to be atelectatic, the likelihood of a bronchial tumor



Fig 5 —Small round cell lymphosarcoma March 4, 1929 Shows a large thymoma in the mediastinum with enlarged cervical lymph nodes, symptoms having developed in a few weeks (Pfahler Am J Roentgen)

being present is great. *Bronchoscopy* and *radiography*, using *opaque oil* as a contrast medium, are the diagnostic methods of choice, although other methods may be required to supplement them. Treatment of a proved bronchial malignancy consists in **excision** or **radiation**, the latter, according to Graham, effecting exceedingly few, if any, cures.

**Mediastinum, Tumors of.**—In a review of 219 cases presenting mediastinal shadows on the x-ray film indicative of tumors, G. E. Pfahler (*Ibid.* 31 458 (Apr) 1934) directs attention to the following causes of mediastinal mass: *enlarged thymus, substernal thyroid, pericardial diverticulum, dermoid cysts, fibromata, lipomata, neuromata, aneurisms*, primary malignant neoplasms and metastatic malignant tumors including: *lymphosarcomata, Hodgkin's disease,*

*leukemic lymphoma, carcinoma and leukosarcomatosis.* Tuberculous and syphilitic *lymphomata* are also encountered, as well as *actinomycosis* and *mycosis fungoides*.

Tumors of the lymphatic variety tend to respond well to irradiation and this therapeutic test may prove helpful.

**Perinephritic Abscess.**—The x-ray diagnosis of perinephritic abscess is discussed by J. H. Shane and M. Harris (J. Urol. 32:19 (July) 1934) who conclude that the x-ray findings in this condition are a valuable aid. Forty cases, proved at operation in the Mayo Clinic, form the basis of their discussion. The *outline of the psoas magnus muscle* on the affected side is more or less obliterated



Fig 6—March 13, 1929 Shows response to a 15 per cent erythema dose of high voltage x-rays, but which was followed by a severe toxemia. (Pfahler: Am. J Roentgen.)

in all cases, while some abnormality of the kidney contour occurs in a high percentage. Scoliosis and elevation of the diaphragm are helpful signs

**Pituitary Gland Tumors.**—P. Puech and L. Stuhl (Presse méd 42:1131 (July 11) 1934) discuss the diagnosis of tumors of the pituitary gland and emphasize the necessity of two special examinations, *ocular* and *radiographic*. *Hypophyseal adenoma* is at first wholly intrasellar and produces no changes demonstrable by x-rays. As the growth increases in size, however, the pituitary fossa undergoes distention and the x-ray picture becomes characteristic. In fact, a certain x-ray appearance of the sella is associated with each variety of adenoma. For example, in cases of *chromophobe tumor*, the fossa is enlarged in all diameters and the clinoid processes are thinned. In cases of *acidophilic adenoma*, on the other hand, distention may be noted in the vertical diameter, but to it are added hypertrophy and elongation of the clinoids. *Tumors of the posterior cranial fossa* are occasionally confusing when they destroy the clivus of the sphenoid and cause an acromegalic syndrome. Differential diagnosis

between hypophyseal neoplasms and *retrochiasmatic arachnoiditis* may be difficult.

**Spondylolisthesis.**—Formerly this condition was regarded as of rare occurrence and largely confined to women who had undergone parturition. Now, however, H. W. Meyerding (Radiology 20 108 (Feb ) 1933), writing from the Mayo Clinic, states his belief that more careful analysis of clinical observations and improved radiological studies have resulted in a correct diagnosis of spondylolisthesis in many obscure cases of *low back pain* that would otherwise have baffled the physician. In a series of 207 patients observed at the Mayo Clinic, 71 per cent were males; 29 per cent. females. The average age was 40 years. Of this series, 86 per cent complained of backache and sacroiliac pain, with or without pain in the legs. A *lateral x-ray examination* establishes the diagnosis and also shows the degree of displacement. If the fifth lumbar vertebra slips forward by less than one-quarter of the distance across the lumbosacral joint, it is graded 1, less than half places the case in grade 2; less than three-quarters, grade 3, and more than three-quarters, grade 4. In extreme cases, operative intervention with bone graft fixation of the third, fourth and fifth lumbar vertebrae and the sacrum may be indicated.

**Stomach, Cancer of.**—W. H. Stewart and H. E. Illick (Am J Roentgenol. 32.43 (July) 1934) relate their experiences with the x-ray diagnosis of *carcinoma* of the *cardiac end* of the stomach and profess their belief that this condition is more frequent in its occurrence than is commonly believed. The x-ray signs of malignant involvement of this area are as follows. Dilatation of the lower third of the esophagus and abnormal retention of the barium meal in this segment, uninterrupted flow of barium through the cardiac orifice instead of the normal delivery in portions, reduction in the esophageal lumen and canalization of the tumor, interference with normal movements in the lower esophagus, esophageal antiperistalsis and gastric hypermobility, demonstration of the tumor mass. *Differential diagnosis* involves the exclusion of cardiospasm, diverticulum, varices, pressure on parts by extrinsic lesions, diaphragmatic hernia, ulcers and adhesions.

**Testicle, Tumors of**—In discussing the differential diagnosis and the treatment of tumors of the testicle, R. B. Henline (J Urol 32 177 (Aug ) 1934) states that a quantitative estimation of *prolan A* (the sex-hormone of the anterior lobe of the pituitary gland) excreted in the urine of patients with testicular neoplasm may make a prompt and correct diagnosis. Following this, the degree of radiosensitivity of the growth may be determined by again estimating the sex-hormone after a full erythema dose of x-rays applied to the tumor, groins and lower abdomen. A sharp decline in prolan A excretion indicates the presence of a radiosensitive neoplasm.

**Urography.**—P. Constantinesco (J d'urol 38 97 (Feb ) 1934) emphasizes the importance of careful procedure if the interpretation of intravenous urograms is to be satisfactory.

(1) The patient must be properly prepared by having all gas and fecal material removed from the intestinal tract. (2) An adequate number of plates must



be exposed. Economy of plates may lead to error. (3) A reliable contrast medium should be employed. Abrodil and its derivatives are preferred at the present time. (4) Ureteral compression is of great service in improving the shadows caused by the eliminated dye.

Close collaboration between urologist and roentgenologist is essential to the best diagnostic work.

**RADIUM AND X-RAYS.—THERAPEUTIC USES.—***Introduction.*—A general survey of the application of radium and the x-rays during the past year in the treatment of *malignancy* indicates a progressive clarification of attitude on the part of the medical profession with reference to the utility of these therapeutic agents, either alone or in conjunction with surgery. Statistics issuing from leading clinics clearly demonstrate the vital importance of adequate radiotherapeutic facilities in the hands of a competent staff of specialists trained in the theoretic and practical fields of radiology. In discussing this subject, A. C. Christie (J. A. M. A. 103:985 (Sept 29) 1934) calls attention to the fact that the cause of cancer being unknown, the treatment is still in large measure empirical, and this accounts for the constant evolution observed in methods of combating malignancy. Summarizing current procedures in irradiation of two of the most important types of *carcinoma*, *cervical* and *mammary*, Christie states: "The following general procedure, recommended by William P. Healy, which is now widely used, has gradually evolved from extensive experience:

"1. Roentgen irradiation of the entire pelvis with high voltage and heavy filtration, spread over suitable time; this recognizes the importance of dealing first with metastases into the regional lymphatic areas and of preventing dissemination of the disease from subsequent manipulation of the local lesion

"2 Approximately 10 days after completion of the roentgen series, the radium treatment in the vagina and cervix is begun. Applicators containing radon or radium well filtered (0.5 mm of platinum or equivalent and rubber) are placed against the cervix and in the lateral fornices for a total dosage of from 3000 to 4000 millicurie or milligram hours. This deals with the superficial cervical lesion and extensions into the base of each broad ligament.

"3 A day or two after the vaginal application, tubes in tandem are inserted into the cervical and uterine canal for a total dosage of about 3000 millicurie or milligram hours.

"4 About a month or 6 weeks after the beginning of the treatment the patient is carefully examined for any small remaining lesions, and these are treated by the interstitial application of radon seeds or small radium needles

"The following points with regard to the treatment of *carcinoma of the breast* are now quite generally accepted among experienced radiotherapists

"1. The initial treatment in all cases of breast carcinoma should be a thorough course of high voltage roentgen irradiation over the breast and lymphatic drainage areas, a total dosage of about 5000 roentgens spread over at least 3 areas over a period of 21 days.

"2 If the tumor is inoperable because of fixation, extensive glandular involvement, the age of the patient or the type of the cancer (inflammatory type,

cancer *en cuirasse* or acute duct carcinoma), the subsequent treatment will depend on the condition present from 6 to 8 weeks after the roentgen treatment. In very extensive involvement the palliation resulting from the initial treatment may be all that it is possible to accomplish. In others it is often possible to destroy localized nodules or ulcer by interstitial application of radon or radium. Much can be accomplished in seemingly hopeless conditions for the comfort of the patient and prolongation of life.

"3. If the tumor is operable, the logical time for operation is from 6 to 8 weeks after the roentgen irradiation. Nothing but good is accomplished by this delay; the devitalization of cancer cells and sealing the vascular channels greatly lessens the liability of dissemination of the disease at the time of operation. Preoperative irradiation in breast cancer as a routine measure is undoubtedly a real advance in treatment of this disease. When the roentgen treatment is administered by the Coutard method, the injury to normal structures is not such as to create any difficulties or untoward complications in the operation.

"4. The question of postoperative irradiation is in a somewhat unsettled condition at present. There is good evidence that it has substantially increased the percentage of cures over what is possible with the radical breast operation alone. Now that the more rational method of preoperative irradiation is coming into use, the question must arise as to the necessity for additional irradiation after operation. If the preoperative irradiation has been given to the point of maximum tolerance, as it should be in all cases, care must be exercised in administering subsequent radiation therapy. The important point is that the total amount of radiation, preoperative and postoperative combined, must remain well within the tolerance of the normal structures."

**Acne Vulgaris.**—Any therapeutic procedure that will prove of benefit in the treatment of so common and so obstinate a cutaneous affliction as acne vulgaris is worthy of careful study and thorough trial. B. H. Sherman (Radiology 21:465 (Nov.) 1933) relates his experiences with the radiation treatment in this condition and emphasizes the fallacy of depending upon any one line of attack to the exclusion of other methods. *Basic causes* should be sought for and corrected when found. If systemic disturbances are present, such as menstrual or gastrointestinal disorders, focal infections or glandular dyscrasias, these should be thoroughly investigated and proper treatment applied. Apropos of this phase, the comprehensive study of a large group of students in a leading University by R. L. Cunningham and C. J. Lunsford (California and West Med 35:22 (July) 1931) is of timely interest. They found that

1. Acne lesions are found more frequently on the backs of young women than on their chests and more frequently on their chests than on their faces.

2. More young women in the 15 to 24 age-group have acne than in the 25 to 34 age-group.

3. Nutrition, as expressed in weight deviation from a selected standard, is not a determining factor in acne incidence.

4. Complexion is without significance when the amount of acne present is considered.

5. There is no relation between the presence or absence of acne in the 15 to 24 age-group and such menstrual characteristics as age of beginning, duration, irregularity of interval, amount of pain, or amount of flow.

6. A history of boils, constipation, appendicitis, and tonsillitis has no appreciable bearing on the incidence of acne.

7. Foci of infection in the nose and throat may favor the development of acne.

8. Thyroid enlargements are associated with a slight increase in acne incidence.

Sherman divides cases of acne into 4 groups, on the basis of clinical differences, as follows: (1) *Comedo type*, characterized by an oily skin, blackheads, and the development of a few papules and pustules. This variety responds very favorably to x-radiation. (2) *Erythematous type*, less amenable to treatment by x-rays and usually demanding close scouting of underlying systemic disorders with a view to their correction. (3) *Papular type*, exhibiting particularly comedones and papules about the hair follicles. These usually are quite amenable to radiotherapy. (4) *Acne indurata*, characterized by indurated subcutaneous masses that contain pus or cystic material and are essentially chronic and persistent. Prominent scars remain when the masses are evacuated. Here, x-rays are of great value, though it should be borne in mind by both physician and patient that as pustules and indurations are cured, scars thereby become more conspicuous and really constitute the principal disfigurement. Sherman emphasizes the necessity of making photographs of the affected area before commencing treatment so that progress may be readily estimated and scars, if they appear, correlated with the original lesions. The technic of the x-ray therapy comprises an initial dose of one-fourth of a skin unit twice a week, using unfiltered rays. During the next 4 or 5 weeks, one-third skin unit per week is administered through 2 mm. of aluminum.

An alternate method consists in giving fractional unfiltered treatments, although the permanent installation of a 1 mm. aluminum filter is regarded as a prudent policy.

**Actinomycosis.**—R. Stewart-Harrison (Brit J Radiol 7.98 (Feb) 1934) reviews 30 cases of actinomycosis treated by irradiation, in each one of which the diagnosis had been established by microscopy. The head or neck showed involvement in 22 of the cases, while in 8 the disease was present in the lungs or other organs. Protracted daily radiotherapy, employing small doses, was used with success in the head and neck cases.

**Bladder, Cancer of.**—B. S. Barringer (Surg Gynec. Obst 58 867 (May) 1934) relates his experiences with 78 controlled cases of cancer of the bladder, most of which were treated by radium at the Memorial Hospital in New York. He finds that there appears to be no relationship between the grade of a tumor and its radiosensitivity, and that determination of grade by the pathologist is not particularly helpful in planning treatment. External radiation alone has proved disappointing in controlling bleeding from a malignant growth in the bladder; therefore, it is unreasonable to expect a cure from this form of therapy unaided by other means. Barringer believes that the implantation of radon seeds of 1

to  $1\frac{1}{2}$  mc. placed a little less than 1 cm. apart constitutes the ideal plan of treatment and that a **suprapubic cystotomy** with this implantation is a relatively benign procedure. The following tables illustrate in striking fashion the force of the writer's conclusions:

TABLE I  
RADIOSENSITIVITY OF BLADDER TUMORS

	Radio-resistant	Radio-sensitive
Grade I	1	2
Grade II	17	13
Grade III	8	10
Grade IV	1	3

TABLE II  
MORTALITY OF CYSTOTOMY OPERATION AND RADIUM IMPLANTATION

Number of cystotomy operations	179
Number of deaths in hospital	13
Mortality per cent	7.2

TABLE III  
TIME WELL IN YEARS—78 CASES

0-1	6
1-2	8
2-3	4
3-4	12
4-5	6
5-10	31
10-15	10
15-20	1

TABLE IV  
CASES OPERABLE OR INOPERABLE IF SURGICAL REMOVAL WERE CONSIDERED

	Cases
Operable	33
Inoperable	43
Borderline	2

TABLE V  
THREE AND FIVE-YEAR CURES—205 PERSONAL CASES

	Cases	Per cent
Well 3 years	56	27
Well 5 years	39	19

**Bone, Metastasis to.**—From time to time the advisability of administering therapeutic irradiation to the bone metastases of carcinoma is questioned. A. Pickhan (Deutsche med. Wchnschr. 60: 132 (Jan. 26) 1934) believes that such treatment is highly desirable even though permanent cures are not obtained. The palliation is so satisfactory and the benefits so great that they bear comparison with the results seen in the x-ray treatment of the leukemias and Hodgkin's disease.

**Breast, Cancer of.**—The radiation therapy of cancer of the breast is discussed by G. W. Grier (Pennsylvania M J. 38: 19 (Oct.) 1934) under the following heads: (1) Radiation without operation; (2) preoperative radiation; (3) postoperative radiation; (4) radiation of recurrences. In regard to the first class of cases, Grier feels that all operable tumors should be removed surgically. Inoperable growths should not be regarded as hopeless and therefore irradiated in a half-hearted way, because thorough, well-planned x-ray treatment will occasionally yield a result comparable to that produced by successful surgery, and, in any breast cancer patient over 65 years of age, the expectancy of life with radiotherapy is quite as good as that with surgery when all hazards are taken into account. **Preoperative irradiation** of the cancerous breast, advocated by Boggs in 1912, appears never to have come into general use, although Pfahler has frequently recommended it and B. J. Lee has stated that it has improved his 5-year results. Grier advocates a full dose of x-rays (generated at 200 K V) over the breast, axilla and supraclavicular region, with surgical removal following recovery of the patient from her radiation sickness. If operation is postponed for 2 or 3 weeks, the secondary x-ray changes in the irradiated tissues delay healing. The late development of lymphatic chemical fibrosis requires protracted x-ray treatment and this does not seem a rational procedure at all.

In regard to **postoperative radiotherapy** of the cancerous breast, Grier calls attention to the conflicting opinions expressed by Harrington, a surgeon, and Pfahler, a radiologist. The former states his belief that malignant recurrences take place just as often in cases irradiated postoperatively as in those that are not. The latter, on the other hand, finds that radiotherapy as applied by him results in  $2\frac{1}{2}$  times as many recoveries as occur by operation alone. In this connection Grier sagely remarks that it is the radiologist who cures the patient, not the x-ray machine.

Obviously, an uncertain factor in **postoperative radiation** is the fact that no one is able to tell whether or not malignant cells are actually present at the beginning of the treatment. Grier's routine technic comprises 135 K V x-rays directed to the breast area and axilla and 200 K V rays over the supraclavicular region. Each area receives 3 or 4 applications after the saturation method to produce the equivalent of 3 or 4 erythema doses. Small repeated doses are regarded as ineffective in destroying cancer cells, and their action upon normal tissue is distinctly deleterious. Recurrences in the cutaneous and subcutaneous tissues are usually sensitive to radiation unless they have been allowed to progress to the stage of ulceration. Low voltage x-rays rather lightly filtered are indicated here, although a recurrence in the form of a large, thick, indurated area should be attacked at once with high voltage rays, 1000 to 1100 r being applied at the

initial sitting and subsequent irradiations of 500 to 600 r being employed at intervals of 2 weeks until a total dose of 3000 r has been reached. Metastases are always more radioresistant than are their parent growths, and distant metastases are practically always heralds of a fatal outcome. Nevertheless, intensive treatment with x-rays generated at 200 K. V. should be used, as the palliation is often most gratifying.

J. C. Bloodgood (Radiology 22:651 (June) 1934) expresses his opinions upon the utility of pre- and postoperative irradiation in cancer of the breast. As a postoperative and postbiopsy form of therapy, he believes it should be the



Fig 7—Photograph made March 13, 1931. Illustrates a female, aged 48, with enlarged cervical glands on left side of neck extending from ear down to clavicle, with a raised scar running through its center. Two years previously patient was treated by a cancer quack with pastes and poultices over a period of 7 months. Microscopic examination on March 30, 1931, showed tuberculous adenitis. X-ray treatment. A total of 285 per cent S. E. D., divided into 6 treatments, was given over a period of 45 days. Observation on May 25, 1931, found patient free of all swelling and scar smooth. (Pfahler and Kapo. Am J Roentgen.)

exception and not the rule. Patients with *inoperable cancer en cuirasse* benefit by **radiation** and this should be the treatment of choice, not operation plus radiation. A patient presenting herself with a clinically benign breast tumor which, upon excision and microscopic examination is pronounced doubtful, should receive immediate radiotherapy, and this should be continued upon the supposition that the growth is a malignant one.

L. J. Carter (Canad. M. A. J. 30:173 (Feb.) 1934) reviews 120 consecutive and unselected cases of *mammary carcinoma*. These all received **x-ray therapy** combined with **surgery**, and of this number (excluding 30 patients that failed to cooperate in receiving radiotherapy and 24 that had not yet passed the 5-year

period), 26 survived for more than 5 years, while 10 survived more than 10 years. Carter is a strong advocate of pre- and postoperative x-radiation in cancer of the breast.

Arcelin (Lyon méd. 152:461 (Oct. 29) 1933) advocates **x-ray** therapy applied to *bone metastases secondary to carcinoma of the breast*. When pain is present, the first effect of adequate treatment is the marked relief obtained. Two or three months later, radiographic evidence of calcification and repair of the involved bone areas may be obtained. In the case of vertebral metastases,



Fig 8—Photograph taken on August 3, 1931, shows improved result (Pfahler Am. J. Roentgen)

Arcelin employs 600 r over each of 2 posterior portals during a period of 2 weeks. A second course of irradiation may be administered later

**Cervical Adenitis.**—G. F. Pfahler and P. J. Kapo (Am J. Roentgenol 32:293 (Sept) 1934) review their experiences with 333 consecutive cases of cervical adenitis treated by means of the x-rays. It is to be noted that the lymphatics form a kind of collar of superficial nodes encircling the neck and comprising the occipital, mastoid, preauricular, facial, submental and submaxillary nodes and the faucial and pharyngeal tonsils. A deeper chain of nodes, named the carotid, lying under the upper four-fifths of the sternocleidomastoid muscles receives the drainage from all of the above; the tonsils drain directly into the anterior carotid; the adenoids drain into the posterior set.

Common *causes* of benign, inflammatory enlargements of the cervical glands are: Tonsillopharyngitis, dental disease, otitis media, scalp pediculosis, scarlatina,

mumps, measles, influenza and diphtheria. The tonsil is the usual source of the infection. In any case of cervical adenopathy, the nasopharynx should always be subjected to close scrutiny, since a small, primary malignant nodule may be present. If examination of the neck of the patient excites a suspicion of metastatic malignancy, then a biopsy should be performed after preliminary radiation.

*Differential diagnosis* involves taking into account Hodgkin's disease, lymphosarcoma, leukemia, syphilis, tuberculosis and bronchial cysts.

**X-ray therapy** is directed to the affected area and the following factors are used: 130 K. V., 5 ma, 40 cm, skin-target distance, 6 mm. aluminum filter, and 50 per cent. skin-erythema-dose (300 r). This is repeated at 1 or 2 week intervals until the desired result is obtained. Often 2 applications are sufficient, but it is not deemed prudent to give more than 10 applications.

Pfahler and Kapo are convinced of the superior value of x-radiation in cervical adenitis and state that the majority of patients can probably be cured in from 2 to 4 treatments. If *old sinuses* and *thickened red scars* complicate the case, these may be successfully treated by **electrothermic destruction**.

**Dermatitis, X-ray.**—In writing upon the treatment of x-ray dermatitis occurring on the hands, W. S. Handley (Lancet 1:120 (Jan 20) 1934) recommends a **complete axillary and bicipital lymph gland extirpation** if these nodes are palpable. He places little reliance on a negative pathological report, **inasmuch** as the microscopic section may not pass through that part of the excised node which contains the metastatic growth. The surgical procedure comprises amputation of the affected fingers or parts of the extremity and dissection of the above mentioned lymph nodes, together with the intervening deep fascia that carries the lymphatic vessels.

**Esophagus, Cancer of**—This is generally conceded to be one of the most hopeless types of malignant disease and cures by any known means are not expected in the overwhelming majority of cases. Nevertheless, any procedure or combination of procedures offering palliation is well worthy of serious consideration and painstaking trial. In discussing this problem, L. Ducuing (Rev. de laryng 54:470 (Apr) 1933) observes that surgical attack upon the growth is futile except in the case of tumors limited to the cervical portion, and even here the results are discouraging. In 35 cases cited by von Winwarter, the operative mortality was nearly 50 per cent and there were 12 rapid recurrences. One patient survived 18 months. **Gastrostomy** should be performed on all patients incapable of easily swallowing liquids, in order to prevent dehydration and loss of general resistance. Ducuing then introduces flexible esophageal sounds carrying **radium** tubes, which are properly placed under fluoroscopic control. An average applicator contains 3 tubes of 5 mg. each, which remain *in situ* for a total of 260 to 300 hours during a period of 15 to 20 days. In addition, surface applications of radium are made externally. He has obtained no cures by this method, but feels that the palliation obtained is well worthwhile.

C. Blumensaat (Deutsche Ztschr. f. chir. 241:654, 1933) states that patients suffering from carcinoma of the esophagus may expect a prolongation of life for 6 to 12 months following a combination of **x-rays** and **radium** therapy and a



**gastrostomy.** He reports 32 cases and believes that none of these has had any untoward local reaction resulting from the radiation.

A series of 89 cases of esophageal cancer treated by radiation are reported by F. J. Cleminson and J. P. Monkhouse (Proc. Roy. Soc. Med. 27: 365 (Feb.) 1934). Of these, 6 had involvement of the upper 3 inches; 28, the lower 3 inches; 55, the intermediate section of 4 inches. **Radium** was applied by means of an **intracavitary application**. The duration of life following treatment averaged 5.6 months for the whole series.

**General Irradiation.**—In connection with the current discussions relative to the therapeutic value of x-rays administered to the *entire body* over protracted periods of time, the contribution of L. F. Craver and W. S. MacComb from the Memorial Hospital, New York, is of timely interest (Am J. Roentgenol. 32: 654 (Nov.) 1934). The radiation from a Coolidge tube operating under a potential of 185 K. V. is directed into a *special ward* containing 4 beds. Two of the beds are at a distance of 5.4 meters from the tube target; the other two are at 7.3 meters. Two mm. of copper constitute the metallic filter, while the high tension current volume is 3 ma. The intensity of the radiation arriving at the nearer pair of beds is 17 r per hour, measured in air. The other beds receive 0.9 r per hour. Male patients are exposed to the rays for an average of 20 hours a day; female, for a somewhat shorter period. Calculating on the basis of 20 hours a day and estimating a clinical skin erythema as produced by 750 r measured in air, at a single exposure of high voltage x-rays, the time required to administer a 30 per cent. erythema dose (or 225 r) to a patient in a bed 7.3 meters distant from the target of the tube works out at 250 hours. If the patient receives 20 hours of irradiation per day, then obviously he must remain for 12.5 days.

Craver and MacComb summarize their experiences with 134 cases so treated and state that it is a procedure of decided value when dealing with several radio-sensitive tumor processes, such as *lymphosarcoma*, *multiple myeloma*, *Hodgkin's disease* and the *leukemias*. In cases of chronic lymphatic leukemia and pseudo-leukemia, it has proved superior to local irradiation as ordinarily administered.

**Hyperthyroidism.**—The effects of **x-rays** upon the normal and pathological thyroid are discussed by A. A. Gallino (Semana Méd. 41: 345, 1934) and he reports 26 cases of hyperthyroidism treated by irradiation. He considers that this method is the best except in cases of Basedow's disease showing grave cardiac complications or pronounced pluriglandular disturbances and those cases with tumoral compression. Many patients that remain uncured following surgery are benefited by irradiation. Gallino remarks that x-ray therapy of the thyroid is harmless, has no mortality, does not subject the patient to emotional stress, and does not interfere with subsequent operation if the latter becomes necessary.

**Inflammatory Disease, Superficial.**—A. B. Friedman (Am J Surg 25: 107 (July) 1934) reviews the results obtained by employing therapeutic **x-rays** in 1018 cases of superficial inflammatory disease, comprising *lymphangitis* and *cellulitis*, *carbuncle* and *furunculosis*, *acne* and *erysipelas*; *breast abscess*, *parotitis*, *paronychia* and *Ludwig's angina*. *Osteomyelitis*, *adnexal disease* and *mastoiditis* were also treated. All of the above mentioned conditions were benefited by the irradiation except osteomyelitis. Friedman believes that this form of

therapy is highly beneficial, but is not as widely recognized and practiced as it should be. It proves curative in early cases and definitely shortens the clinical course in more advanced ones. An increase in antibodies in the irradiated tissue is believed to be the basis of the favorable response. Comparatively small doses of low K. V., weakly filtered x-rays are employed.

**Laryngeal Tuberculosis.**—S. Attilj (Radiol. Med. 21:224 (Mar.) 1934) reports his experiences with 13 cases of tuberculous laryngitis treated by applications of the **x-rays**. Some of the physiological disturbances resulting from the tuberculous involvement showed prompt subsidence. This was particularly true of the dysphagia and dysphonia. The laryngeal lesions regressed in every case and in 4 disappeared entirely, although in 2 cases the general condition of the patient became worse on account of advancing pulmonary disease. Attilj believes all forms of tuberculous laryngitis are amenable to radiotherapy but that the best results are obtained in cases showing the *paretic-congestive syndrome* with infiltration confined to the true or false cords and the posterior third of the larynx. Improvement is least in cases with extensive tuberculous ulceration

**Leukemia, Myelogenous.**—In discussing the radiotherapy of myelogenous leukemia, U. V. Portmann (J. A. M. A. 102:178 (Jan 20) 1934) states his belief that the benefit derived depends in large measure upon the degree of aplasia or actual atrophy of erythropoietic tissue caused by invasion of the red bone-marrow. All x-rays, from the longest to the shortest, and all radium rays affect certain white blood cells, which they eliminate from the circulating blood. The technical factors governing the production of the radiation are not of great importance so long as the latter is therapeutically effective in the parts of the organism where it is absorbed

It should be borne in mind that *splenomyelogenous leukemia* becomes sooner or later a generalized disease, although the chief sites of hemocytogenesis are in the vertebrae, ribs and sternum, the long bones being of secondary importance. Hence, irradiation should be primarily directed to the more important areas of blood cell formation. An enlarged *spleen*, when annoying, should receive direct treatment, in the early stages of enlargement, the response is gratifying, later, when fibrosis has developed, the effect of radiation may be disappointing. Likewise, reduced renal function indicated by unfavorable changes in the blood urea and in phenolsulphonephthalein elimination may be considerably improved by judicious irradiation of the *kidneys*. Portmann considers that x-rays directed to the general circulating blood have no influence upon the production of the abnormal white cells in the bone-marrow. He has observed only a temporary reduction in the white cell count.

**Melanoma of Skin.**—In reviewing 50 cases of malignant melanomata, T. Butterworth and J. U. Klauder (*Ibid.* 102:739 (Mar. 10) 1934) find that these tumors are relatively uncommon. They vary in histological structure, and the transition from a benign to a malignant pigmented growth may occur at any age. This change may be indicated by increasing size and pigmentation of a mole in association with tendency to hemorrhage. Biopsy is hazardous, as it may induce metastasis. Butterworth and Klauder believe that the treatment of choice consists in **surgical excision** followed by **high voltage x-rays** directed to the

tumor site and all regional lymphatic drainage areas. They regard cauterization of pigmented moles as dangerous in that this procedure may lead to malignant degeneration.

**Nasopharyngeal Fibromata.**—A. Santoro d'Emidio (Riv. oto-neuro-oftal. 10:76 (Jan-Feb.) 1933) notes the pronounced tendency toward *hemorrhage* shown by nasopharyngeal fibromata, which, as a rule, are highly vascular. Surgical removal may precipitate bleeding of a sufficient gravity to require ligation of the external carotid, besides failing to insure the patient against recurrence of the growth. While improved results have been reported following electrocoagulation, the writer believes that **radium** is the best therapeutic agent for employment in these cases. He introduced 2 tubes containing 10 mg. element each and sufficiently filtered to remain *in situ* for 8 to 11 days. The response of the tumor is most gratifying and the profuse hemorrhage avoided.

**Oral Cavity, Cancer of.**—Attention is called by C. L. Martin (Radiology 22:136 (Feb.) 1934) to the fact that almost all cancers of *lip*, *mouth* and *pharynx* are of the epidermoid or squamous cell type and that such tumors require from 6 to 12 erythema doses of irradiation to effect a cure. An earnest effort should be made to produce a cure with the first series of treatments, since the second is invariably less successful, as well as disposed to cause certain injurious reactions in the normal structures.

In attacking carcinoma of the *lip*, Martin administers 1 or 2 erythema doses of lightly filtered **x-rays** of relatively long wavelength every day or every other day until a total dosage of 6 to 12 erythemata has been reached. A pronounced reaction occurs, but subsequently subsides, and healing is usually accomplished in from 6 to 8 weeks. Biopsy is usually omitted in lip lesions, as it is feared metastasis may be induced by this procedure, and the cosmetic results are also less favorable following tissue removal. When dealing with lip cancer that has been previously subjected to inadequate radiation, Martin employs weak **radium needles** implanted under the tumor margins for 7 days.

*Intraoral carcinoma* presents a decidedly more difficult problem than does carcinoma of the lip, because metastases occur early and prove highly resistant. If a large neoplastic mass develops in the *cheek*, a row of small **radium needles** is sewn around the margin inside the mouth, while a series of long needles is inserted under the growth externally. Martin emphasizes the necessity of insisting upon rigid **oral hygiene**, comprising frequent **mouth-washing with an antiseptic solution** and painting of the affected area with 2 per cent **mercurochrome** at least thrice daily. Intraoral and *pharyngeal tumors* are fairly radio-sensitive, as a rule. In treating the latter, the **Coutard plan** is followed, half an erythema dose being delivered over the same neck area daily, for a total of 10 or 12 doses.

In dealing with *metastasis to the cervical lymph nodes*, Martin recommends **block dissection** if the nodes are operable. When inoperable, **radium needles** are inserted beneath and beyond the involved area and allowed to remain for 7 days. A 100 mg. pack with 1 mm. platinum filtration and an air-gap of 2 cm. is also applied over the affected nodes for 36 hours. In addition to the interstitial and external radium therapy, **x-rays** generated at 200 K. V. are administered



Fig 9 —Cancers of lower lip, all of which have remained well for 3 years or more. Treatment consisted of x-rays alone in each instance. (C. L. Martin: Radiology )

in sufficient quantity to ensure an erythema dose to both sides of the neck from the superior maxillæ to the clavicles.

*Cancer of the tongue* is regarded as a particularly intractable form of malignancy and rightly so, in view of its pronounced tendency to recur after surgical removal. Nevertheless, E. S. Judd and J. R. Phillips (Proc. Staff Meet. Mayo Clin. 9:8 (Jan. 3) 1934) cite 4 selected cases in order to prove that the disease is curable even after it has become extensive. Case 1 was treated by **cautery removal** of the primary growth with **block dissection** of the corresponding side of the neck and **excision** of the submental and submaxillary **nodes**. A local recurrence was removed 3 months later. Pathological report: squamous cell carcinoma, Grade III. Patient was well 21 years later. Case 2 has a recurrent, Grade II squamous cell carcinoma that was **excised surgically** together with a **dissection of the draining lymph nodes**. Patient was free of disease 21 years later. Case 3, with a recurrent cancer was subjected to a **wide removal of the growth by cautery**. Patient was alive and well more than 20 years. Case 4 showed an extensive and ulcerated carcinoma on the lower aspect of the tongue. **Cautery excision** with **bilateral node dissection** was carried out. A local recurrence 8 years later was treated by **surgical diathermy**. Patient is now free of the disease after 14 years. The current procedure at the Mayo Clinic when dealing with lingual cancer is to remove the primary growth by **diathermy**. If this is extensive, **radium** is inserted into the operative wound. Cancers of the base of the tongue receive radium by implantation provided they are not suitable for diathermy on account of their extent. Routine **dissection of regional lymphatics** is also carried out and if the **nodes** are found to contain metastatic deposits, **external radiation** is employed.

F. Perussia (Radiol. med. 21:921 (Aug.) 1934) believes that the results of **surgery** and of **radiotherapy** are essentially the same when dealing with *carcinoma* limited to the anterior part of the *dorsum* of the *tongue*, the *gums* and the *mandible*. Cancer of the *lips*, *palate* and *floor* of the *mouth* responds better to **radiation** than to surgery. Operable growths of the *cheeks*, *base* of the *tongue* and *tonsils* are likewise more amenable to **radiotherapy**. **Operative intervention** is indicated in the case of small *cylindromata* of the *palate*, *adenocarcinomata*, and carcinoma with a high degree of differentiation. Perussia recommends the administration of very large doses of **x-rays** or **radium**, except, of course, under circumstances where such treatment is contraindicated, as in cases of severe sepsis or advanced cachexia.

Cancers of the *pharynx*, *tonsil* and *extrinsic larynx* present peculiarly difficult problems when surgical extirpation is proposed. These growths, too, are frequently highly resistant to irradiation as ordinarily applied, so that any improvement in the radiotherapeutic procedures merits careful consideration. The **divided dose technic** introduced by **Coutard**, of Paris, about 15 years ago and developed by him to a point where tremendous dosage can be administered through multiple daily treatments without inflicting irreparable damage upon mucosa and skin, appears to have accomplished more with these growths than has any other form of **radiotherapy**.

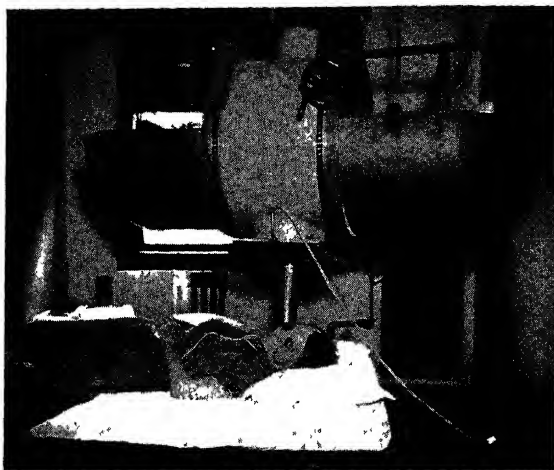


Fig 10—Case of carcinoma of antrum being treated through a metal cone, 7 cm. in diameter. (Martin and McNattin. Am J Roentgen)



Fig 11—Carcinoma of tonsil 3 days after completion of  $2 \times 3,000$  r at 200 kv over a period of 20 days, and healed condition in about 6 weeks (Martin and McNattin Am J Roentgen)

H. E. Martin and R. F. McNattin (Am. J Roentgenol 32 717 (Dec ) 1934) relate their experiences at Memorial Hospital with the divided dose technique employed in 140 cases. They believe the essential features of this technique, as used by Coutard, to be as follows

- 1 The treatment should be given daily and should be of equal quantity unless the clinical course indicates a raising or lowering of the daily doses
- 2 A total treatment period of a definite length (15-20-30 days, etc ), in which to deliver a certain total dosage should be decided upon. This treatment period should be adhered to unless the clinical course indicates that it should be shortened or lengthened
- 3 In most cases of intraoral or pharyngeal cancer, the total biological effect produced must be close to the local and general tolerance, in that definite blistering of the skin and a mucositis must be produced in order to approach a lethal effect on most tumors

The technique employed at Memorial Hospital aims to deliver about 4000 r units (at 200 K V.) to each side during a series of 20 daily treatments (Sundays excepted). The results obtained in 140 cases are shown in the following table.



RESULTS OF SEPTEMBER 1, 1933, FOR CASES TREATED DURING THE YEARS 1931 AND 1932.

Years	Number of Cases Treated	Extrinsic Larynx			Tonsil			Naso- pharynx			Pharynx and Soft Palate			Base of Tongue			Intrinsic Larynx			Anterior Floor of Mouth			Total Per Cent. Free of Disease	Survival Period
		Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease	Cases Treated	Number Free of Disease	Per Cent Free of Disease		
1931	73	31	5	16	24	9	31	9	3	33	3	0	0	4	0	0	1	1	100	1	1	100	19 Cases—26%	1¾ to 2½ yrs. 9 mo. to 1¾ yrs.
1932	67	22	5	22	17	4	23	12	4	33	6	3	50	6	3	50	2	1	66	1	1	100	22 Cases—32.8%	
Total .	140	53	10	19	41	13	31	21	7	33	9	3	33	10	3	30	4	3	75	2	2	100	41 Cases—29%	

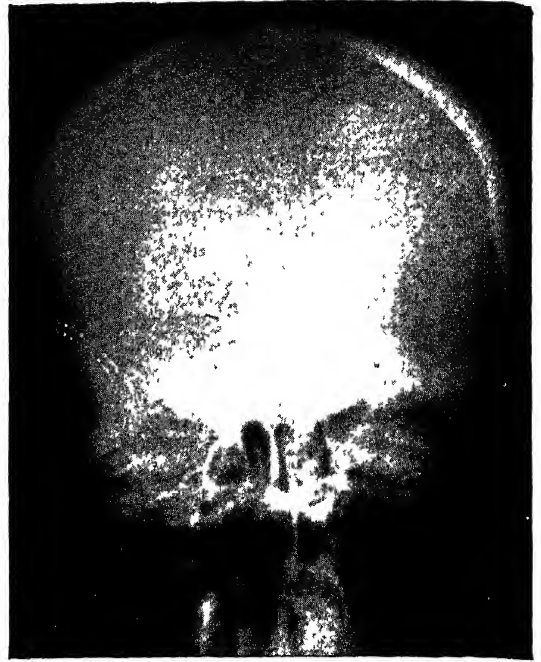
*B**A*

Fig 12—(*A*) Skull, anterior view Before treatment September 19, 1932 (*B*) Skull, anterior view After treatment July 13, 1933 (Cutler and Owen Surg., Gynec and Obst )

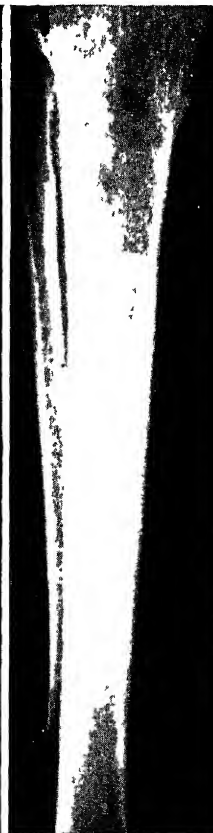
*A**B*

Fig 13—(*A*) Tibia, right. During treatment, January 5, 1933 (*B*) After treatment September 6, 1933 (Cutler and Owen Surg., Gynec and Obst )



***Osteitis Fibrosa Cystica.***—M. Cutler and S. E. Owen (Surg Gynec. Obst. 59:81 (July) 1934) report their experiences with **x-radiation** directed to the **parathyroids** in the treatment of osteitis fibrosa cystica. In this disease a *high blood-calcium* figure may be encountered and x-ray control of the parathyroid activity is then indicated by a drop in this figure accompanied by improvement in the bone lesions, as shown by an increased deposition of lime salts in the cystic areas. It is worthy of note that normally functioning glands are quite resistant to irradiation (as evidenced by the absence of tetany in patients receiving enorm-



Fig. 14—(A) Femur right Before treatment September 23, 1932 (B) After treatment September 6, 1933 (C) Femur left Before treatment September 23, 1932 (D) After treatment July 13, 1933 (Cutler and Owen Surg. Gynec. and Obst.)

ous doses for carcinoma of the thyroid or the larynx), but the hyperplastic or adenomatous or malignant glands are relatively sensitive. Cutler and Owen cite a case of osteitis fibrosa cystica responding brilliantly to radiotherapy of the parathyroids, as shown in the accompanying radiographs.

***Ovary, Cancer of.***—J. B. Montgomery and J. T. Farrell, Jr. (Radiology 23:157 (Aug.) 1934), review their experiences with **postoperative x-ray therapy** applied to 22 cases of ovarian carcinoma. Four of these were adenocarcinomata, 3 were papillary adenocarcinomata, 1 was a granulosa-cell carcinoma, and 14 were papillary cystadenocarcinomata. X-ray therapy was instituted from 2 to 4 weeks after operation and an attempt made to deliver a depth dose

of 1600 to 2000 r within a month. The palliation and prolongation of life obtained varied with the histological grade of malignancy exhibited by the individual tumor, but demonstrated the value of irradiation as an adjunct to surgery in this type of malignancy.

The results of irradiation in the treatment of papillary ovarian tumors are discussed by S. Simon (*Strahlentherapie* 46:444, 1933) and, inasmuch as the multiple peritoneal implants from these parent growths have been known to undergo spontaneous regression, the effects of radiotherapy are naturally subject to controversy. Simon cites 4 cases that received **x-rays** or **radium**, or both, as the primary treatment. Of these, 2 have remained well for 5 and for 8 years, respectively. The other two succumbed to the advance or recurrence of the original malignancy. Two other patients presented bilateral ovarian cancers and were given prophylactic irradiation followed by incomplete surgical extirpation. A 9-year arrest of the disease was obtained in 1 case; the other survived for 5 years and then died of a recurrence.

**Parotid Gland Tumors.**—The treatment of these tumors, benign and malignant, is discussed by A. Hintze (58 *Tag. d. deutschen Ges. f. Chir.*, 1934). During the era of exclusively surgical attack, benign growths responded quite favorably, while the malignant type proved most intractable and the outlook was exceedingly dark. The extensive surgery usually required frequently destroyed the facial nerve, and resection of the external carotid artery, the ramus of the mandible and the external auditory meatus was often performed. At the Surgical Clinic of the University of Berlin, irradiation has steadily grown in favor as the means of choice to be employed in attacking parotid neoplasms. Hintze believes that every parotid tumor, either frankly malignant or under suspicion of being malignant, should be subjected to thorough **radiotherapy**. If a *malignant lymphoma* is present, its response will promptly identify it and it may, at the same time, be cured. If the irradiated growth shrinks to half its size within 6 weeks, then radiation should be kept up. A small residual tumor persisting after **x-ray** treatment may respond to **radium**. If, on the other hand, the parotid neoplasm recedes but slightly after the initial irradiation, total surgical extirpation should be promptly carried out, and the region systematically radiated postoperatively. When dealing with *inoperable malignant parotid tumors*, Hintze employs intensive **x-radiation** followed by **partial extirpation** and subsequent implantation of **radium**. If the process is in an advanced stage, the risk of surgical injury to the seventh nerve is not important, inasmuch as the nerve will eventually be destroyed by the growth itself. *Benign parotid neoplasms* of short duration are best treated by **x-rays**. If the growth, however, has been present for a long time, then size, mobility and location must all be considered in judging the advisability of **surgery**. A history of steady growth, even though this be quite slow, indicates operative removal despite the danger of injuring the facial nerve. Hintze believes that even cases of benign tumors of the parotid should all be given **postoperative irradiation** as a prophylactic.

**Pituitary Gland, Diseases of.**—G. Schulte (*Strahlentherapie* 46:83, 1933) discusses the **x-ray therapy** of diseases of the pituitary gland. He finds that *adenomata* respond favorably to this form of treatment, and that patients suffer-

ing from impairment of vision as the result of these growths, show improved visual acuity. Schulte notes that the following clinical conditions arising from pituitary disease were benefited by hypophyseal irradiation: *acromegaly*, severe *headaches*, *dizziness*, *loss of vision*, *adiposogenital dystrophy*, *amenorrhea* and *sterility*.

**Rectum, Carcinoma of.**—Five hundred cases of primary carcinoma of the rectum treated at the Mayo Clinic are reported by H. H. Bowing and R. E. Fricke (Am. J. Roentgenol. 32:635 (Nov.) 1934) and their response to therapeutic **irradiation** analyzed in the following table:

PROCEDURE	PATIENTS			3-YR. "CURES"		5-YR. "CURES"		10-YR. AND LONGER		TOTAL "CURES"	
	Total	Traced		Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
		Num- ber	Per Cent.								
Surgical with radium	87	87	100	11	12 64	17	19 54	10	11 49	38	43 67
Surgical with radium and x-rays	97	97	100	15	15 62	14	14 58	4	4 17	33	34 37
Surgical with x-rays ..	10	10	100		..	1	10 00	2	20 00	3	30 00
Surgical with radium, x-rays and surgical diathermy . . .	3	3	100	1	33 33	1	33 33	1	33 33	3	100
Surgical with radium and surgical diathermy	1	1	100		..	1	100			1	100
Radium ..	77	74	96 10	4	5 71	1	1 42			5	7 14
Radium and x-rays	211	203	96 20	13	6 59	4	2 03	4	2 03	21	10 61
Radium, surgical dia- thermy ..	4	4	100		..	1	33 33			1	33 33
Radium, surgical dia- thermy and x-rays	1	1	100		..			1	100	1	100
X-rays	9	8	88 88	1	14 28					1	14 28
Total	500	488	97 60	45	9 47	40	8 42	22	4 63	107	22.53

Bowing and Fricke conclude that.

"1. **Surgical intervention** of cases of carcinoma of the rectum, anus and rectosigmoid is most important and should be the first consideration

"2 **Colostomy** is a necessity in some cases It should always be considered as a means of establishing a permanent or temporary opening It is possible to apply adequate radiation treatment in selected cases without colostomy

"3 An attempt should be made to estimate the grade of malignancy in each case and then to decide on a plan of attack

"4. Therapeutic radiology, especially **radium therapy**, has a distinct place in the treatment of carcinoma of the rectum, anus and rectosigmoid

"5. **Preoperative radium therapy** should receive special consideration and, when employed, should be followed by a period sufficiently long, probably 8 to 12 weeks, before surgical intervention is attempted

"6 Radium therapy as a palliative procedure is of value, and inoperable and recurring lesions should be given at least one well planned treatment The degree of palliation naturally varies, but nearly all of the patients will be benefited somewhat

"7. Radium therapy as a postoperative measure has a limited field of usefulness; all lesions of a high grade of malignancy at least should be treated.

"8. **X-ray therapy** is of value, and with the increased voltage of the present day installations, should become of greater value, especially in cases in which lesions are of the higher grades of malignancy.

"9. Since the *rectal polyp* may undergo carcinomatous degeneration, **adequate treatment or removal** of these lesions may be classed as a procedure to prevent the occurrence of carcinoma of the rectum

"10 Owing to the advanced state of malignant involvement of the bowel in the majority of the cases today, as well as the age and general physical condition of the patients, etc., the combined efforts of surgery, therapeutic radiology, and medical treatment should greatly reduce the surgical mortality rate and enhance the initial and late result "

**Skin Tuberculosis.**—Most dermatologists consider the **Finsen light** superior to the x-rays in the treatment of *lupus vulgaris*. M. Buisson (Radiol Med 21 786 (July) 1934), however, advocates the combination of **x-rays** and **moist heat**, the former to destroy the diseased tissue and the latter to promote replacement of the defect thus created by stimulating repair and preventing secondary infection. Buisson employs a maximum dose of 600 to 650 r at 200 K V and follows this with a second treatment after 2 or 3 months. Moist heat is applied in the form of very hot wet compresses placed on the irradiated area and renewed every 2 or 3 minutes for 4 hours a day. A total of 400 to 800 hours of this thermotherapy is delivered.

**Thyroid, Cancer of.**—B. F. Schremer and W. T. Murphy (Ann Surg 99 116 (Jan) 1934) report 42 cases of malignant tumor of the thyroid treated by surgical removal, x-radiation, radium and various combinations of these. They conclude that irrespective of the type of therapy employed, cancer of the thyroid is usually fatal, though fortunately rare. **Early operation followed by irradiation** offers the greatest chance of cure. If the case is sufficiently far advanced to permit clinical diagnosis, the outlook is generally hopeless. Here, **palliative radiation** is employed.

**Uterus, Cancer of.**—H. B. Whitehouse (Surg Gynec Obst 58 447 (Feb) (No. 2A) 1934) recounts his experiences with **radium** therapy in carcinoma of the *uterine cervix* as applied in his own clinic (Birmingham) and also as used in 5 other leading clinics of England and Wales. From 1921 to 1926, 507 women with cervical cancer received radium treatment and the results are given in the following instructive tables.

TABLE I

Year	Years	Incipient	Borderline	Inoperable
1921	10	0	1	0
1922	9	1	0	0
1923	8	3	0	0
1924	7	3	0	3
1925	6	5	4	8
1926	5	8	5	15
Total		20	10	26

TABLE II

	Cases	Per Cent.
Total number of cases treated 1921-1926 ..	34	58.9
Percentage of cures on 5-year basis ..	86	10.6
Total number of borderline cases treated 1921-1926 . . . .	387	6.7
Percentage of cures on 5-year basis . . . . .	56	11.0
Total curability, 507 cases . . . . .		

G. Gellhorn (*Ibid.* 58:879 (May) 1934) describes the technic he employs in irradiating the pelvic contents when dealing with *cancer of the cervix*:

After opening the abdomen by a midline incision, he passes the middle and index fingers of his left hand into the vagina, while his sterile right hand enters the pelvis through the abdominal wound, thus enabling him to make a most thorough bimanual palpation. The extent of the growth having been determined, **radon implants** are inserted beneath the peritoneum in such a way as to completely encircle the periphery of the cancerous area. The guiding fingers in the vagina are of inestimable value in determining sites of implantation and in gauging the depth to which the seeds must be driven. Special attention is given to the iliac triangle and its contained glands, the vesicovaginal septum, the sacrouterine ligaments and the small gland found between the ureter and the uterine artery. Following this procedure, the patient is placed in the lithotomy position and capsules of **radium element** are inserted into the uterine cavity while **radium needles** are also thrust into the tumor itself and along its outer edge.

Gellhorn employs a dosage equivalent to 4200 mg hrs; this, as a rule, is not repeated. He finds the operation borne quite as well as any other laparotomy and without undesirable sequelæ resulting from the irradiation. In addition, some patients are subjected to **x-radiation** 3 weeks prior to the **surgical procedure** in an effort to control the vaginal lymph glands to better advantage.

While upon the subject of cervical carcinoma, it will be pertinent to quote the remarks of H. S. Crossen and G. U. Newell (*Ibid.* 58:450 (Feb.) (No. 2A) 1934).

Present efficiency and future progress in preventing deaths from *cancer of the cervix uteri* are predicated on the following facts:

- 1 The successful care of the patient with cancer of the cervix is based upon an organized combination of expert services. It is the vigorous use and careful coordination of the best that can be secured in several lines that gives the full chance of stopping the malignant process.

- 2 The crucial point of attack is not the uterus, but the cancer cells along the pelvic wall. It is these outlying cells that must be reached and destroyed, or recurrence is certain.

- 3 **Irradiation** is the most important factor in attaining success in this concerted attack on the outlying cancer cells. These are exceptional conditions in which operation also may be advisable, but whenever used, operation should supplement irradiation and not displace it.

- 4 Too many cancer patients are still being treated with half-way measures with operations that never reach the outlying cancer cells, and with inefficient radium and x-ray treatments that carry no devitalization into the distant crucial zone.

- 5 Cancer of the cervix continues to take its high toll of lives in spite of the fact that methods of treatment have been developed to almost complete efficiency for the early stage. The difficulty in raising the average percentage of cures is due to the fact that patients do not come in an early stage, although there has been long and strenuous education as to early symptoms.

The patients do not come early because in the beginning cancer of the cervix is symptomless. In the really early stage there are no symptoms whatever. That is the great obstacle which blocks advance and has for years held the average cures down to between 20 and 25 per cent, while patients with early growths can be cured in 90 to 100 per cent of cases.

Though it is imperative to establish the diagnosis at the earliest possible moment, dependence on early diagnosis for any marked increase in the percentage of cures will prove disappointing. Experience has clearly shown that in most cases of cancer of the cervix there is no warning sign whatever until the cancer spread has become extensive

6. Further marked advance in the prevention of deaths from this form of cancer is blocked until there can be brought about widespread and systematic **removal of those chronic irritative lesions** of the cervix which precede cancer and cause it. Efforts to overcome this serious situation must take into consideration the following facts. Thousands of patients with chronic irritation in the cervix (cervicitis, laceration, eversion, "ulceration," erosion, polyp) are receiving palliative treatment, which may keep them comfortable but does not remove the deep chronic irritation favoring cancer development. Other thousands of women are treating themselves for a "little leukorrhea" in ways that may relieve the discomfort but do not eliminate the lesion. There are still others in which the chronic irritation in the cervix does not give rise to any symptoms that would cause the individual to suspect local trouble. In the attempt to eliminate the chronic irritative lesions, means must be found for reaching these 3 classes of persons

TABLE I  
CLASSIFICATION OF CASES

	Squamous Cell Carcinoma	Adenocarcinoma	Clinical Cases			
			I	II	III	IV
Patients Treated, 121	108	13	3	11	97	10
Survivals 5 to 11 Years, 29	27	2	3	5	21	0

TABLE II  
SECONDARY RADIUM TREATMENTS

	Squamous Cell Carcinoma	Adenocarcinoma	Clinical Cases			
			I	II	III	IV
Patients Treated, 121	108	13	3	11	97	10
Secondary radium treatment—all patients	10	1	0	0	11	0
Secondary radium treatment—survivals	1	0	0	0	1	0

W. P. Healy and A. N. Arneson (Am. J. Roentgenol. 32: 646 (Nov.) 1934) report a series of cases of *cancer of the uterine cervix* treated at Memorial Hospital, New York, by means of a combined irradiation technic comprising direct application of **radium** to the cervix and unusually heavy **x-ray bombardment** of the entire pelvis through alternating skin portals, each portal receiving as high as 2400 r units within a period of 30 days.

The radium therapy consists of 2 radon capsules placed in the cervical and uterine canals for a 3000 mc-hr. dose, the filtration being 0.5 mm. gold and 2

mm. black rubber. Summarizing their experience with this radiotherapeutic procedure, they state:

1. Twenty-five cases of squamous epidermoid cancer and 1 adenocarcinoma, all involving the cervix, were treated with x-rays, 200 r to each of 2 pelvic fields daily for a total of 2000 to 2400 r without severe local or constitutional reactions.

2. Clinical and histological evidence of regression of the cancer in the cervix indicated that regression might also be reasonably expected in the disease in the parametrium for this amount of external x-irradiation.

3. It would seem possible through these observations to plan an x-ray pelvic cycle which will deliver a tissue dosage adequate for control of cancer in the parametrium and outlying pelvic field without severe damage to normal structures.

4. We believe that the opportunity offered to observe the coincident changes in the primary lesion may be utilized to advantage to follow the effects taking place in the parametria.

5. Radium, however, should always be used for treatment of the primary lesion.

6. In the earliest causes, with a small lesion limited to the cervix and without gross enlargement of the cervix, the radium treatment should be carried out before the x-ray cycle is given.

In discussing *cancer of the body of the uterus* W. P. Healy (Surg. Gynec. Obst. 58 452 (Feb.) (No. 2A) 1934) calls attention to the fact that this particular form of malignancy tends to grow slowly and to remain localized within the uterus for a relatively long period of time before it spreads to other structures in the vicinity. Since the average age of women suffering from this type of neoplasm is 55 years and the uterus at this age has become a useless organ, the temptation in the past has been to resort promptly to a hysterectomy. Careful follow-up statistics, however, have clearly demonstrated that less than 50 per cent of 5-year cures were obtained by this method. Healy finds that about half of fundal cancers are *malignant adenomata* and quite slow to metastasize. Here simple surgical **hysterectomy** will usually effect a cure. The other half are true *adenocarcinomata* and metastasize much sooner. Fortunately, however, these are relatively radiosensitive, and, while surgery alone seldom produces a 5-year salvage of over 20 per cent, **radiotherapy** followed by **hysterectomy** will effect a cure in 60 to 85 per cent. of cases. It is important to bear in mind that when serious contraindications to surgery exist in any given case, radiation therapy alone is capable of giving splendid results.

A statistical survey of the results of radiotherapy of *uterine carcinoma* in the Woman's Clinic of the University of Heidelberg is presented by F. G. Dietel (Strahlentherapie 46:201, 1933). Of a total of 542 cases, 446 showed the *cancer in the cervix* and of these, 185 cases were considered operable. Of the *operable* cases, 170 were treated by **irradiation** and 40.6 per cent. of 5-year cures obtained. Coming to the *inoperable cervical* cases, 237 were **irradiated**, with apparent cures obtained in 10.5 per cent. of the number. Ninety-six patients in Dietel's series presented *carcinoma of the uterine corpus*, of these, 87 were deemed operable and 83 of the 87 were given **radiotherapy** with apparent cures in 33.7 per cent.

Dietel advocates **irradiation** as a standard procedure in cancer of the womb, followed by **surgical intervention**, if required, in obstinate cases. For de-

tails of the radiotherapeutic technic the voluminous original article should be consulted.

**Uterus, Fibroid of.**—In relating their experiences with **irradiation** in the treatment of *fibromyoma of the uterus*, G. E. Pfahler and J. H. Vastine (Am. J. Roentgenol. 31: 51 (Jan.) 1934) consider that this is the treatment of choice where the growth extends no higher in the abdomen than the midpoint between symphysis and umbilicus and the patient is near or past the menopause. Furthermore, the fibroid should not be undergoing degeneration nor be giving pronounced pressure symptoms. Women suffering from advanced organic heart disease, nephritis, diabetes, pulmonary tuberculosis or other conditions contra-indicating surgery, should also be treated radiologically. Cases of fibroid that are unsuited for radiotherapy are those complicated by malignancy of the uterus or adnexa or those showing pedunculated or submucous growths. *Large fibroids* causing severe pressure symptoms and yielding too slowly to radiation should be **removed surgically**. In the case of *young women* capable of becoming pregnant and desiring offspring, **myomectomy** is the treatment of choice.

Pfahler and Vastine cite the advantages of x-ray therapy as follows:

(1) Almost universal availability, (2) homogeneous action upon both tumor and ovaries, (3) minimum interference with patient's occupation, (4) economy from the standpoint of expense to the patient, (5) avoidance of an abrupt reaction, (6) absence of caustic action on the endometrium.

When employing radium, they perform a dilatation and curettage first and obtain a pathological opinion on the endometrial scrapings to determine the presence or absence of concurrent malignancy. The intrauterine radium applicator is curved like a sound and carries 2 or 3 50-mg. capsules. Filtration is 1 or 2 mm. of platinum plus 0.5 mm. hard rubber or aluminum. The duration of the application is 24 to 48 hours.

**Uterus, Hemorrhage from.**—L. E. Phaneuf (New England J. Med. 211: 304 (Aug. 16) 1934) is convinced of the value of **radium therapy** in uterine hemorrhages of benign origin and recounts his personal experiences in 150 cases so treated. He divides the patients into 3 groups: (1) Those in adolescence or young womanhood, (2) those in middle life and at the menopause, (3) those past the climacteric. Most cases belong to the second group and it is here that radiotherapy plays its most prominent rôle, particularly as it may well supplant the surgical hysterectomy that formerly was the final resort when dilatation and curettement had failed to control the hemorrhages. The chief contraindications to radium are large fibromyomata, adnexal inflammation and ovarian tumors. The technic consists of introducing a self-retaining catheter into the bladder and placing 50 mg. of radium in the uterine canal with a filter of 1 mm. of brass and a thin rubber sac.

The time of the application varies with the indications of the individual case. Phaneuf feels that

"1. Radium, employed in suitable doses, in properly selected cases, is a valuable agent in the treatment of uterine hemorrhages of benign origin.



"2. It finds its greatest field of usefulness in women near or at the menopause, having severe hemorrhages from uteri showing no gross microscopic lesions, as in hypertrophy and hyperplasia of the endometrium and fibrosis uteri

"3. It should be used cautiously, to avoid hysterectomy, in the hemorrhages of adolescence and only after medical, endocrinal and hemostatic treatment have failed. The dose used should be a very small one.

"4. It should not be used to regulate the menstrual periods and in an attempt to favor pregnancy, because of the risk incurred by the product of conception.

"5. It is of value in treating small fibromyomas of the interstitial type, especially in women nearing the menopause.

"6. It may be used in conjunction with operations for the repair of the cervix, cystocele and rectocele, as it does not in any way interfere with healing.

"7. A single application, giving an appropriate dose, is sufficient to bring on permanent amenorrhea.

"8. The mortality should be *nil* or almost *nil* if the patients are properly selected

"9. These cases may be successfully treated with a small amount of radium (0.050 Gm ) and with a minimum amount of apparatus."



# CLINICAL PATHOLOGY

*by*

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**CLINICAL PATHOLOGY. — ERYTHROCYTES AND HEMOGLOBIN.**—It is generally recognized that frequently repeated observations made on the blood of normal individuals reveal a rather wide degree of variation which is apparently too great to be without physiological or practical significance. O. S. Walters (Am. J. Physiol. 108:118 (Apr.) 1934) studied the effect of muscular inactivity ( $\frac{1}{2}$  hour in a recumbent position) upon the erythrocyte count, hemoglobin and volume of packed cells in 80 healthy men between the ages of 20 and 30 years (Group I). These were compared with similar observations in another group of 80 men after uncontrolled activity (Group II). Comparative observations were also made in 20 cases before and after a period of complete muscular inactivity (Group III).

The resting subjects in Group I showed significantly lower values for red blood cells, hemoglobin, and packed cell volume than did the active subjects in Group II. There was an average drop of 250,000 red cells per c mm. (maximum drop 780,000), of 1.43 Gm. of hemoglobin per 100 c.c. (maximum 3.39 Gm.), of 2.5 c.c. of packed cells per 100 c.c. blood, and of 1.2 per cent. in the mean corpuscular hemoglobin content. In Group III, the red cell count, total hemoglobin and total volume of packed cells showed a significant decrease following the period of complete muscular inactivity, but the corpuscular volume and corpuscular hemoglobin content and concentration were not materially altered. The author believes that the diminution in total circulating hemoglobin and in the volume of packed cells is due to an absolute decrease in the proportion of red blood cells rather than to any alteration in individual cells. He attributes this phenomenon to a withdrawal of red cells into storage depots, especially the spleen.

When subjected to statistical analysis, the differences between the results obtained in the active and in the resting states is too great to be due to chance. According to Walters, these changes probably represent the converse of the erythrocytosis that occurs in association with exercise and emotional states, both phenomena reflecting a delicate balance which appears to adapt the oxygen-carrying capacity of the circulating blood to the requirements of the tissues.

**RETICULOCYTES.**—The number of reticulocytes in the circulating blood is generally regarded as an index of the state of activity of the bone-marrow, or, at least, of its erythropoietic activity. A large number of methods have been proposed for the determination of these important elements of the blood and the upper limits of normal by different methods has varied from 1 to 3 per cent. E. E. Osgood and M. M. Wilhelm (J. Lab. and Clin. Med. 19:1129 (July) 1934) have devised a simple procedure which gives higher values than other methods and which can be used with whole blood.

*Method*—Mix, in a small test-tube, equal parts (5 drops) of oxalated venous or capillary blood and a 1 per cent solution of brilliant cresyl blue in 0.85 per cent sodium chloride. Allow to stand for 1 minute, then mix and make thin smears, which are dried in air. The reticulocytes may be counted in the usual manner in these preparations at any time within 24 hours. If permanent preparations are desired, the slide must be counterstained with Wright's or some other blood stain by the usual technic. The brilliant cresyl blue solution keeps well but should be filtered if any sediment appears on the slide. If the reticulocyte count is above 5 per cent, only 500 red blood cells need be counted, if below 5 per cent 1000 cells should be counted.

In a study of 110 normal men and 50 normal women, the authors found that the percentage of reticulocytes ranged from 0.5 to 3.8 per cent., averaging 1.57 per cent., the sex variation being relatively slight and of no practical significance. When calculated on the basis of total numbers of reticulocytes, however, the following figures were obtained: males, 26,050 to 211,660, averaging 83,160 per c.mm.; females, 21,400 to 156,800, averaging 72,800 per c mm. These values are considerably higher than those usually stated as normal by other methods. The authors believe that the normal range by this method should be regarded as 0.4 to 4 per cent. and that the results should be expressed in terms of percentage rather than total number of reticulocytes.

**BLOOD IN NORMAL PREGNANCY.—Hematology.**—W. J. Dieckmann and C. R. Wegner (*Arch. Int. Med.* 53:71 (Jan.), 188 (Feb.) 1934) made repeated determinations of blood and plasma volume and hemoglobin, hematocrit and erythrocyte values in women at different times during the course of normal pregnancy and in the puerperium. The observed changes were as follows:

- 1 The blood and plasma volumes began to increase in the first trimester, the increase amounting to 16 and 18 per cent., respectively, at the thirtieth week. The average increase in blood volume at term was 23 per cent., and in plasma volume 25 per cent. At 8 weeks postpartum there was an average decrease of 16 per cent. in both factors.

- 2 There was a definite decrease in hemoglobin concentration, the lowest level, averaging about 15 per cent. below normal, being reached between the twenty-sixth and thirty-fifth weeks. At 2 weeks postpartum the hemoglobin was 17 per cent. and at 8 weeks 14 per cent. below normal.

- 3 The changes in hematocrit values were similar to those in hemoglobin, the maximum decrease being 14 per cent., recovery was somewhat more rapid than in the case of hemoglobin and the same was true of the erythrocyte count.

- 4 Although the total amount of circulating hemoglobin showed an average increase of 13 per cent. and the total cell volume an average increase of 20 per cent., owing to the greater increase in plasma volume these factors were relatively decreased.

- 5 The authors regard a hemoglobin content of less than 10 Gm. per 100 c.c. during the course of pregnancy as indicative of anemia.

**Plasma Cholesterol.**—W. J. Dieckmann and C. R. Wegner (*Ibid.* 53:540 (Apr.) 1934) made simultaneous repeated determinations of plasma cholesterol and plasma volume in women at different periods of pregnancy, with the following results.

- 1 There were marked variations in the plasma cholesterol concentration in individual cases at different times during the course of pregnancy. In the majority of cases there was an increase which became apparent at 10 to 15 weeks' gestation. This increase amounted to an average of 23 per cent. at term, an average decrease of 27 per cent. being noted 8 weeks postpartum.

- 2 The average increase in the total cholesterol content of the plasma was 33.9 per cent. at 26 to 35 weeks of gestation and 27.9 per cent. at term. A con-

stant decrease occurred after delivery, amounting to 21.2 per cent at 8 weeks postpartum.

According to E. M. Boyd (J. Clin. Investigation 13:347 (Mar.) 1934), the lipemia of pregnancy is due almost entirely to an increase in plasma lipids, the red cells showing but little change and examination of whole blood giving little indication of what is taking place. The neutral fat of the plasma began to increase in the first trimester and phospholipid and cholesterol in the second. At term the increase in neutral fat amounted to over 100 per cent. and that in phospholipid and cholesterol (free) about 25 per cent. Boyd believes that although there is at present no adequate explanation for the lipemia of pregnancy, this condition probably belongs in the group of similar persistent lipemias which includes diabetes and experimental anemias.

**PLASMA CHOLESTEROL.**—*Diabetes Mellitus.*—The increase in plasma cholesterol which occurs in diabetes mellitus has attracted considerable attention in the past few years, particularly from the standpoint of its significance in prognosis and treatment. The essential cause of diabetic hypercholesteremia has not been clearly understood. Recently, E. B. Man and J. P. Peters (J. Clin. Investigation 13:237 (Mar.) 1934) reported observations on the cholesterol, fatty-acid and lipid phosphorus content of the serum of patients recovering from diabetic acidosis which throw some light upon this problem. It was found that contrary to the generally accepted concept of a parallelism between serum cholesterol and fatty acids in diabetic lipemia, the cholesterol, at the height of acidosis, was never more than 60 per cent. above the upper limit of normal, while the nonphospholipid fatty acids exceeded the maximum normal limit by 200 per cent in 4 cases and by 400 per cent. in one instance. The concentration of cholesterol was independent of the severity of the acidosis. The concentrations of all of these components fell during the acute phase of recovery and comparison of the lipoids with the proteins of the serum indicated that a large but variable proportion of this diminution was referable merely to hemodilution. The course of cholesterol paralleled that of protein more nearly than did the course of the fatty acids, while phosphatides occupied an intermediate position, the variations of cholesterol apparently bore little relation to those of the fatty acids.

With few exceptions, the concentrations of cholesterol found in the serum in acidosis were of a magnitude compatible with the conception that hemoconcentration is the chief cause of the hypercholesteremia in this condition. Occasionally, extremely high values are obtained which must be dependent upon other factors, but none were observed in the present study. On the other hand, the marked increase in fatty acids during acidosis and their marked diminution during the recovery period cannot be attributed so definitely to alterations in the water content of the serum. It would appear that these changes in fatty acids are due largely to alterations in carbohydrate metabolism. These studies emphasize the necessity of evaluating more critically changes in plasma cholesterol concentration in diabetes and of taking into consideration the factor of hemoconcentration in interpreting abnormalities in the concentration of individual components of the blood plasma or serum. They also illustrate the fallacy of relying entirely

upon cholesterol determinations in investigating abnormalities of lipid metabolism in diabetes.

**Hyperthyroidism and Hypothyroidism.**—Reference was made in these pages a year ago to the rather consistent occurrence of hypocholesteremia in hyperthyroid states. It was noted that there appeared to be a roughly reciprocal relationship between the elevation in the basal metabolic rate and the lowering of the blood cholesterol in individual cases. W. C. Cutting, D. A. Rytand and M. L. Tainter (*J. Clin. Investigation* 13: 547 (July) 1934), applying statistical methods to 205 cases reported by a number of observers, found that there was a significant, inverse, curvilinear correlation between the basal metabolic rate and the blood cholesterol in thyroid disorders. They found, however, that this correlation was not present when the basal metabolic rate was increased by dinitrophenol and concluded, therefore, that the changes in blood cholesterol in thyroid disease are not directly related to the metabolic rate but to other actions of thyroid secretion.

The value of plasma cholesterol estimations in thyroid disease is further emphasized by the studies of L. M. Hurxthal (*Arch. Int. Med.* 53: 762 (May) 1934) upon patients with myxedema and other hypothyroid states. Myxedema, whether occurring spontaneously or following thyroidectomy, or x-ray therapy, was quite consistently accompanied by varying grades of hypercholesteremia, values as high as 680 mg. per 100 c.c. having been obtained in such cases. The author states that hypercholesteremia, when not explainable on any other basis, may be regarded as possibly of thyroid origin. He believes that this finding, in the absence of its other relatively few causes, points more specifically to thyroid deficiency than does the finding of a subnormal basal metabolic rate.

**MAGNESIUM IN BLOOD PLASMA.**—The rapidly growing tendency to investigate the nutritional significance of mineral elements has in recent years extended knowledge of the physiological and pharmacological significance of magnesium. The methods in common use for the determination of this element in the blood are time-consuming and rather cumbersome. A. D. Hirschfelder and E. R. Serles (*J. Biol. Chem.* 104: 635 (Mar.) 1934) describe a simple adaptation of Kolthoff's colorimetric method for the determination of magnesium in biological fluids which is free from these disadvantages and is sufficiently accurate for clinical use.

**Reagents.**—The distilled water and other reagents must be free from magnesium and calcium, *i. e.*, they must give no trace of pink when tested with NaOH solution plus a drop of the dye, and no turbidity with ammonium oxalate.

1. NaOH solution, approximately 0.4 N (16 per cent).
2. Dye solution. Titian yellow or Clayton yellow, 0.01 Gm. per 100 c.c. of H<sub>2</sub>O.
3. Ammonium oxalate solution, 3 per cent.
4. Colloid dispersing agent. An approximately 0.5 per cent suspension of soluble starch or C. P. dextrin. The contents of a No. 1 gelatin capsule just filled with the powdered starch ( $411 \pm 7$  mg.) or dextrin ( $415 \pm 10$  mg.) may be taken as a sufficiently accurate amount. This is transferred to a mortar, ground to a paste with a little cold water, and then gradually diluted to 80 c.c. This solution must be freshly prepared.

**Standard Magnesium Solutions.**—For the determination of magnesium the color produced by diluted alkalinized plasma is compared with that produced by 0.0002 per cent magnesium (0.002 mg. per c.c.). Such a standard solution is too dilute to be preserved and is therefore prepared freshly as described below.



5. Standard 1 Exactly 1 Gm. of bright magnesium ribbon is weighed and dissolved in concentrated HCl. For this purpose 5 c.c. of HCl are added and when solution is as complete as possible, more is added drop by drop until solution is complete. Dilute to 1000 c.c. with water. Add 2 c.c. of chloroform as a preservative. Whenever the odor of chloroform has disappeared, 1 c.c. of chloroform should be added and the bottle shaken vigorously.

6. Standard 2. Dilute 2 c.c. of Standard 1 to 100 c.c. with water. To 1 c.c. of this diluted standard add 7 c.c. of colloid-dispersing agent, 1 c.c. of 0.01 per cent. dye solution, and 1 c.c. of 0.4 N NaOH solution. The tube is stoppered and mixed thoroughly by inversion. This standard must be freshly prepared (1 c.c. is equal to 0.002 mg. of Mg.).

*Procedure*—Place about 5 c.c. of blood in a 15 c.c. centrifuge tube containing a few small crystals of sodium citrate, stopper with a rubber stopper, mix by inverting 3 times, and centrifuge at 1500 R. P. M. for 15 minutes. Pipette 1 c.c. of plasma into a graduated centrifuge tube, add 0.5 c.c. of 3 per cent. ammonium oxalate solution and 8.5 c.c. of H<sub>2</sub>O at 45° C. Stopper; mix thoroughly by inversion, place in a water bath at 45° C. for 20 minutes and centrifuge for 15 minutes.

Place 5 c.c. of the supernatant fluid in a test-tube, and add 3 c.c. of dispersing colloid agent, 1 c.c. of dye solution and 1 c.c. of 0.4 N NaOH solution. Mix thoroughly and compare in a colorimeter with Standard 2. The light used should be filtered through a color screen of 0.01 per cent dye solution. As a container for this solution use an oblong glass vessel about 25 cm. long, 15 cm. deep, and 1 to 2 cm. thick.

*Calculation.*— $\frac{\text{Reading of Standard}}{\text{Reading of Unknown}} \times 4 = \text{mg of Mg per 100 c.c plasma.}$

If the plasma Mg is too high to be determined in the range of the colorimeter, the mixture used for comparison with the standard must be diluted further and the calculation revised accordingly.

The authors also describe a modification of this procedure which may be employed for the accurate determination of magnesium and calcium in 0.1 c.c. of plasma.

The normal concentration of magnesium in the plasma ranges from 1.8 to 2.5 mg per 100 c.c., averaging about 2 mg. A. D. Hirschfelder (*Ibid.* 104:647 (Mar.) 1934; J. A. M. A 102:1138 (Apr. 7) 1934) found that when normal individuals take Epsom salt by mouth, about 40 per cent. of the ingested magnesium is excreted in the urine within 24 hours, the concentration of magnesium in the plasma being practically unaltered. He made the important observation, however, that in the presence of renal functional impairment the administration of one or more purgative doses of Epsom salt may result in hypermagnesemia with, at times, profound symptomatic manifestations. These consist mainly of varying grades of psychic and neuromuscular depression, drowsiness at times occurring with plasma magnesium concentrations of about 8 mg per 100 c.c., and coma with values of about 12 mg per 100 c.c. In animals, coma occurred whenever a level of 17 mg per 100 c.c. was reached.

The author believes that many cases of coma in patients with nephritis, regarded as uremic in origin, may be dependent upon a state of hypermagnesemia induced by the administration of magnesium sulphate. He states that a single ordinary dose of Epsom salt by mouth may raise the concentration of magnesium in the blood plasma of patients with nephritis to 9 to 11 mg per 100 c.c., about two-thirds of the concentration at which coma sets in in experimental animals. It seems probable that even more dangerous levels may be attained by the repeated administration of this commonly used substance. Since the same probably is true

of magnesium citrate, these purgatives should be avoided in the treatment of individuals with renal functional impairment, sodium sulphate being the saline of choice in such cases.

**SERUM PHOSPHATASE.**—The increasing realization of the clinical significance of determinations of serum phosphatase activity has led to the development of technical methods the performance of which is of sufficient simplicity to be clinically available. The procedure most widely employed in the past has been that devised by Kay or one of its various modifications. According to A. Bodansky (J. Biol. Chem. 101: 93 (June) 1933), this method is unsatisfactory, the source of greatest difficulty being the 48-hour period of incubation specified by Kay. Variable retardation by products of hydrolysis occurred in analyses of plasma or serum high in phosphatase and the limits of the method were frequently exceeded. Bodansky proposes the following procedure, which has been applied with satisfactory results in the laboratory of the reviewer :

**Solutions.—Buffered Substrate**—Dissolve 25 Gm. of sodium glycerophosphate (the beta-glycerophosphate obtained from either the Boots Pure Drug Co., Ltd, Nottingham, England, or the Eastman Kodak Research Laboratories) and 212 Gm. of monosodium diethylbarbiturate (Merck's barbitol-sodium U S P X) in a 500 cc volumetric flask. This substrate is preserved in the refrigerator in glass-stoppered bottles (100 to 250 cc) under a layer of washed petroleum ether (b p 30 to 36°) about 3 cm thick.

**Ten Per Cent Trichloroacetic Acid Solution**—Baker's analyzed

**Reagents for Inorganic Phosphorus Determination**—Standard phosphate solution (5 cc equivalent to 0.02 mg. of P), freshly prepared acid-molybdate reagent; freshly prepared dilute stannous chloride solution (0.3 per cent)

**Procedure**—Measure 10 cc of substrate (equivalent to about 5 mg. of P) into a test-tube 18 or 20 mm. by 150 mm., avoiding aeration of substrate, place it in a water bath at 37° C. for a few minutes, add 1 cc of centrifuged serum, mix by a single inversion and replace in the water bath for exactly 1 hour. When an incubator is used, a beaker of warm water should be employed for preheating the substrate to 37° C. Remove, cool immediately in ice water, add 9 cc of 10 per cent trichloroacetic acid; mix and filter after a few minutes through Whatman filter paper No. 44 (11 cm.) or similar paper of low ash content ("total inorganic P filtrate," each cc equivalent to 0.05 cc of serum). Use 1 cc of serum (1.5 or 2 cc if the inorganic phosphorus is expected to be less than 3 mg.), precipitated with 9 volumes of 5 per cent trichloroacetic acid, to obtain the filtrate for an inorganic serum phosphate analysis. The filtrates may be saved in the refrigerator until analysis, analyses performed immediately and after several days yield excellent checks.

Calculate the inorganic phosphorus content of each filtrate, the total inorganic P after incubation minus the serum inorganic P equals the liberated inorganic P. The results are stated in units per 100 cc of serum, a unit of phosphatase activity being defined as equivalent to 1 mg. of P liberated from a sodium glycerophosphate substrate as the phosphate ion during the first hour, at pH 8.6 and at 37° C.

According to the author, interpretation of clinical results may be facilitated by the following summary: normal adults, 15 to 40 units per 100 cc; generalized osteoporosis, 5 to 10 units; clinical hyperparathyroidism, about 25 units, localized Paget's disease of bone, 5 to 20 units; polyostotic Paget's disease, 50 to 135 units; normal children, 5 to 12 units; active rickets, 30 to 165 units, healed rickets, 6 to 14 units. Serum phosphatase is generally increased in jaundice (see p. 1008).

G. Stearns and E. Warweg (*Ibid.* 102:749 (Oct.) 1933) report observations on the phosphatase activity of the serum of 124 children ranging in age from birth to maturity. The average was low at birth, but rose rapidly and abruptly to a maximum during the first month. This maximum level was maintained only a short time, although the average value remained at a comparatively high level until well into the second year of life. The average level during middle childhood and adolescence was toward the upper limit of the normal adult range.

**SEDIMENTATION TEST.**—Intensive investigation in recent years has resulted in the demonstration of several factors which influence the “suspension stability” or sedimentation rate of red blood cells. Among these are temperature, the number and volume of red blood cells, the nature of the anticoagulant employed, and the time elapsing between the withdrawal of the blood and the performance of the test. The importance of anemia in increasing the rate of sedimentation was emphasized particularly by Rourke and Ernstene, who described a method of correcting the observed rate in anemic blood to that which would have occurred in the presence of a red blood cell volume of 45 per cent (packed cells). This was termed the “corrected sedimentation index.”

D. R. Gilligan and A. C. Ernstene (*Am. J. M. Sc.* 187:552 (Apr.) 1934) studied the relationship between the sedimentation rate and the fibrinogen content of the blood plasma of normal individuals and patients with various pathological conditions. They observed a close correlation between these two factors, the rate of sedimentation (corrected sedimentation index) varying directly with the plasma fibrinogen concentration. However, in certain cases with intrahepatic damage, the increase in the sedimentation index was greater proportionally than that in fibrinogen.

The authors believe that their observations indicate that, except in conditions associated with liver damage, the plasma fibrinogen concentration plays a major rôle in controlling the corrected sedimentation index. They state that the explanation for this relationship must reside in the physicochemical properties of fibrinogen in respect to its effect upon red blood cell aggregation.

H. W. Sulkowitch (*Ibid.* 187:65 (Jan.) 1934) describes a photographic apparatus for the automatic, graphic demonstration of the rate of sedimentation which depends, in principle, upon the difference between plasma and whole blood in their penetrability to light rays. Light is projected through the plasma in a blood-filled hematocrit tube upon light-sensitive photographic paper on a drum in constant motion. As the red blood cells sediment, the increasing height of the column of acellular plasma is automatically recorded on the sensitized paper. When this is subsequently developed and fixed, it presents an accurate and continuous record of the rate of sedimentation of the red blood cells. The advantages of this apparatus are that it is self-recording, requires no attention after it is started, and gives results that are free from possible errors dependent upon the personal equation of the observer.

**HETEROPHILE ANTIBODIES IN ACUTE INFECTIOUS LYMPHOCYTOSIS.**—The significance of heterophile antibodies (agglutinins and hemolysins) in the blood of individuals with acute infectious lymphocytosis (mononucleosis) was first emphasized by Paul and Brunnell in 1932. These sub-

stances had previously been found only in persons to whom horse serum had been administered. A. Bernstein (J. Clin. Investigation 13: 419 (May) 1934) described a method for determining the presence and titer of heterophile agglutinins as follows:

**Materials.**—(1) Patient's serum, (2) a suspension of sheep cells; (3) physiologically normal salt solution.

**Procedure.**—The patient's serum, obtained as for any agglutination reaction, is inactivated at 56° C. for 15 minutes; if kept in an ice-box, its potency, as far as agglutinins are concerned, remains constant for several months. Dilutions of serum, beginning at 1:4, are carried out as far as is indicated. Sheep cells are collected weekly, the cells being washed 3 times and prepared as a 2 per cent. suspension of packed cells. To each tube containing 0.5 c.c. of diluted serum, add 0.5 c.c. of the 2 per cent. suspension of sheep cells and 1 c.c. of normal salt solution, bringing the total volume to 2 c.c.

The tubes are shaken and placed in a water bath at 37° C. for 1 hour. They are then allowed to remain overnight in the ice-box. On the following morning the tubes are inverted 3 times, after which the results are recorded as follows: Single mass of cells, + + +; large flakes, + +; small flakes, +; barely macroscopic agglutination ±.

Application of this test to 300 hospital patients with a variety of conditions other than acute infectious lymphocytosis never revealed an agglutination titer exceeding 1:16. In 13 of 15 cases of infectious lymphocytosis examined in the acute stage, agglutination occurred with serum dilutions as high as 1:4096. Except in these cases, agglutination titers above normal were observed in only 3 patients, one of whom had previously received horse serum containing heterophile antigen. In a subsequent report (*Ibid.* 13: 677 (July) 1934), Bernstein found a low heterophile antigen titer in the blood of 21 patients with leukemia, being less than 1:4 in 2 instances. In the majority of conditions which may simulate leukemia clinically the distribution of agglutinin titers was much wider, ranging to 1:16. Among these conditions were leukemoid reactions in acute infections, miliary tuberculosis, thrombocytopenic purpura, agranulocytic angina, aplastic anemia, Hodgkin's disease, lymphosarcoma, erythroleukemia and carcinomatous, tuberculous or syphilitic involvement of the lymph nodes. The determination of the heterophile agglutinin titer of the blood appears to afford a ready and fairly certain means of diagnosing acute infectious lymphocytosis in its early stages, at a time when its differentiation from acute or subacute forms of lymphatic leukemia may be very difficult.

**GONOCOCCI, CULTIVATION OF.**—J. W. McLeod, J. C. Coates, F. C. Happold, D. P. Priestley, and B. Wheatley (J. Path. and Bact. 39: 221 (July) 1934) describe a method for the cultivation of gonococci involving an oxydase reaction described by them in 1928 and incubation in an atmosphere rich in carbon dioxide.

**Medium.**—Ten per cent heated blood agar prepared from a bouillon obtained by extracting 1 pound of minced meat with 1000 c.c. of a 1 per cent solution of peptone and 0.2 per cent  $\text{Na}_2\text{HPO}_4$  at 60° C. for 45 minutes, followed by 30 minutes in a steamer. The reaction should be pH 7.4. Then add the minimum quantity of agar required to impart stability to the medium.

**Procedure.**—Incubate for 18 hours at 36° C. in a closed jar which has previously been filled with a mixture of 8 per cent. carbon dioxide and atmospheric air. Remove and incubate for 24 hours in an open incubator.

*Recognition of Colonies.*—The plate is covered with a 1 per cent. solution of tetramethyl-p-phenylenediamine hydrochloride which is run off immediately. Medium-sized convex and translucent colonies which rapidly become bright purple are accepted as colonies of gonococci if they consist of Gram-negative diplococci.

The authors point out the fact that ordinary smear methods may show Gram-negative diplococci other than gonococci, so-called "pseudo-gonococci." They state that direct microscopic examination, apart from its failure to detect gonococci in some cases proven positive by cultural methods, may be responsible for falsely positive diagnoses in 1 to 5 per cent. of cases. Over a period of about 3½ years, positive cultures were obtained by the above method in 14.5 per cent. of 2062 cases examined, only 7.75 per cent. being correctly diagnosed by direct microscopic examination of smears.

**TUBERCULOSIS, DIAGNOSIS OF.**—The diagnosis of tuberculosis by means of the demonstration of tubercle bacilli in the sputum is notoriously difficult in children, in whom frequently little or no sputum can be obtained for examination, particularly in early stages of the disease. A distinct advance was made in this connection by Meunier who, in 1898, first suggested that the stomach contents be examined for tubercle bacilli in such cases. Recently, I. Gourley (*Am. Rev. Tuberc* 29 461 (Apr) 1934) reported the results of the examination of stomach washings in 59 children by smears and guinea-pig inoculation

The stomach was washed with 50 to 200 c c of normal salt solution in the morning after a fast of at least 6 hours. All but one gave a positive reaction to 0.1 mg. of old tuberculin, injected intradermally; the one exception reacted to 1.0 mg. The bacteriological studies were negative in 31 (52.6 per cent.) of the 59 cases and positive in 28 (47.4 per cent.). Of the negative group, 22 showed some x-ray evidence of pulmonary tuberculosis and 9 did not. All those with positive bacteriological findings showed x-ray evidence of pulmonary tuberculosis, but in some instances the lesions were so slight or apparently so well healed that these findings were entirely unexpected. The bacteriological findings in the positive x-ray group were classified as follows: (1) parenchymal involvement (20 cases), 15 positive and 5 negative, (2) enlarged hilum or mediastinal lymph nodes (18 cases), 8 positive and 10 negative; (3) calcified lesions (12 cases), 5 positive and 7 negative.

There was no indication in these cases of any other portal of entry of tubercle bacilli into the gastrointestinal tract. This study appears to indicate that all types of parenchymal tuberculous lesions in children, including the "C" group of McPhedran (supposedly with negative sputum), are open cases.

A similar study was made by L. Mishulow, C. Kereszturi and D. Hauptman (*Ibid* 29 471 (Apr) 1934), involving bacteriological examination of feces, stomach washings and sputum in 60 tuberculous children. Tubercle bacilli were found in smears from the feces in 12 cases (20 per cent.) and from the stomach washings in 16 (26.6 per cent.). Of the 44 specimens obtained by gastric lavage which were negative by smear examination, 4 gave positive results by guinea-pig inoculation. Thus, a total of 20 cases (33½ per cent.) yielded positive bacteriological findings.

The authors state that guinea-pig inoculation should always be employed as a final confirmatory measure in cases in which smears are negative, and they stress the importance of repeated examinations at different times. It is stated that positive findings are obtained in 83.3 per cent. of patients with destructive and over 24 per cent. with nondestructive parenchymal lesions.

J. P. Nalbant (*Ibid.* 29:481 (Apr.) 1934) found that 7 of 19 children with no demonstrable pulmonary tuberculosis showed tubercle bacilli in the gastrointestinal tract upon culture and guinea-pig inoculation. They enumerate the possible sources of the bacilli in the gastrointestinal tract as follows: (1) lungs (swallowed sputum); (2) receding childhood type of pulmonary tuberculosis with negative x-ray findings; (3) caseation of a tracheobronchial lymph node with erosion into the trachea, bronchi or esophagus; (4) infected bile; (5) tuberculous enteritis or gastritis; (6) tuberculous otitis media, sinusitis or tonsillitis; (7) tuberculoma of a bronchus or bronchiole. In the present series, the second source seemed most probable, *i. e.*, a receding primary pulmonary lesion of the childhood type with negative x-ray findings.

**RENAL FUNCTION TESTS.—Urea Clearance.**—The widespread employment of the urea clearance test in the estimation of renal functional efficiency has resulted in the elucidation of several factors which may influence the rate of removal of urea from the blood stream. Certain of these were reviewed in the last SUPPLEMENT. C. L. Cope (*J. Clin. Investigation* 12:567 (May) 1933) and, more recently, W. Goldring, L. Razinsky, M. Greenblatt and S. Cohen (*J. Clin. Investigation* 13:749 (Sept.) 1934) have investigated the effects of alterations in the protein intake upon the urea clearance in normal subjects and nephritics. It was found that a decrease in the protein content of the diet from 75 to 40 Gm. per day was accompanied by a lowering of the urea clearance in nephritic patients with essentially normal clearance values during the control periods. In the studies made upon patients without renal, cardiac or vascular diseases, the protein was varied from 9 Gm. to 280 Gm. per day, 100 Gm. being administered during the control period. An average reduction in clearance of 23 per cent. was noted during the period of low protein intake (9 Gm.), the greatest diminution being 36 per cent. No significant increase in urea clearance accompanied an increase in protein intake from 100 Gm. to 280 Gm. These observations in normal subjects and in patients with nephritis emphasize the necessity for taking into consideration the protein intake in interpreting results obtained by the urea clearance test.

M. N. Fulton, H. A. Van Auken, R. J. Parsons and L. F. Davenport (*J. Pharmacol. and Exper. Therap.* 50:223 (Feb.) 1934) investigated the influence of various diuretics upon the elimination of urea. Among the substances employed were salyrgan, ammonium chloride, novasurol, digitan, urea, theocin, caffeine citrate and diuretin. Although there was a marked degree of variation in the quantities of urea excreted in the urine, no consistent change was noted in the blood urea clearance values following the administration of any of these diuretic agents. F. S. Fowweather (*Quart. J. Med.* 3:63 (Jan.) 1934), however, reported a distinct and quite constant increase in urea clearance following the administration of 15 Gm. of urea. His conclusions, based upon observations upon 50 healthy

students and 43 hospital patients, 20 of whom had some form of renal disease, were as follows:

1. The urea clearance of subjects without renal disease was much more constant after giving 15 Gm. of urea than before and the values obtained occupied a narrower range than under the conditions of the test as ordinarily performed.

2. The results obtained suggest that blood-urea clearance after urea is a more correct index of the state of renal functional efficiency than the urea clearance before urea.

3. Whereas 28 per cent of the normal group showed values below 70 per cent. of the accepted average normal by the procedure ordinarily employed, none fell below 70 per cent. of the average normal following the administration of urea.

4. Although the difference was less pronounced, patients with renal disease usually showed higher values following the ingestion of urea than before.

5. The following procedure was suggested for the performance of the urea clearance test: "At 7 A. M. the patient may be allowed a light breakfast; coffee must be avoided, but tea, if weak and in small quantity, may be permitted. At 9 A. M. the bladder is emptied, and immediately thereafter the urea is given (15 Gm. in about 200 c c of water). At 10 A. M. the bladder is again emptied. At about 10:45 A. M. a specimen of blood is taken for urea determination, and at 11 A. M. the bladder is again emptied. . . . The clearance value is . . . calculated from data obtained from the third urine specimen (exact volume, exact time of excretion, to nearest minute, and urea concentration) and the blood specimen."

It should perhaps be pointed out that recent observations indicate that the prohibition of coffee, tea and other diuretic substances during or before the test period is apparently unnecessary.

H. T. Karsner, R. F. Hanzal and R. A. Moore (Arch Path 17:46 (Jan) 1934) found that unilateral nephrectomy is followed by a transient period (up to 6 months) during which the remaining kidney is physiologically deficient; subsequently the urea clearance values return to normal. During the period of impaired function, the extent of the functional insufficiency was exaggerated when the test was performed following the administration of urea. These observations are in accord with those previously reported by L. B. Ellis and S. Weiss (Am J M Sc 186:233 (Aug) 1933).

**Plasma Cholesterol Concentration.**—On the basis of their studies of the cholesterol content of the blood plasma in patients with chronic nephritis and retention uremia, B. J. Ashe and M. Bruger (Am J. M. Sc 186:670 (Nov.) 1933) arrived at the following conclusions:

1. In cases of chronic nephritis with marked nitrogen retention, a low plasma cholesterol presages death in uremia, low values being usually observed several days before death.

2. An elevated plasma cholesterol concentration indicates a good immediate prognosis as to recovery from the pre-uremic state.

3. There appears to be no close relationship between the level of plasma cholesterol and the degree of edema in nephritic patients.

4 There is some evidence of a roughly reciprocal relationship between the blood urea and the plasma cholesterol but not between the latter and the plasma proteins.

5. The diminished cholesterol content of the plasma in such cases is probably dependent largely upon associated factors, such as cachexia and anemia

Data collected in the laboratory of the reviewer are in accord with those of Ashe and Bruger. Cholesterol values as low as 48 mg per 100 c c have been obtained in patients with advanced renal functional insufficiency. Although the reciprocal relationship between the blood nonprotein nitrogen and cholesterol was not found to be constant, nevertheless increase in the former was usually associated with diminution in the latter, and *vice versa*, in individual cases. The reviewer feels that a fall in the plasma cholesterol concentration, which is usually somewhat elevated during the compensated stage of renal disease, is of definitely serious prognostic significance

**HEPATIC FUNCTION.**—In a review of hepatic function in relation to hepatic pathology, F C Mann (Ann Int Med. 8 432 (Oct ) 1934) made the following observations:

1 Although the serum bilirubin concentration is frequently a valuable index of the efficiency of the pigment-excretory function of the liver, it is often unsatisfactory as a quantitative index of the degree of hepatic injury. (One of the most important of the extra-hepatic factors that affect the serum bilirubin concentration in hepatic disease is the amount of hemoglobin available for the formation of bile pigment, which, in turn, depends upon the rate of blood destruction, loss of blood and diet Furthermore, immediately following obstruction of the common bile duct in animals, the serum bilirubin concentration rises to relatively high levels and then subsequently falls to low levels in the later stages of biliary stasis despite the presence of extensive hepatic damage

2 In studying the relationship between microscopic changes in the liver in experimentally produced cirrhosis and the degree of dye retention (bromsulphalein), it was found that, in general, the extent of pathologic change in the hepatic cells appeared to parallel the degree of retention of the dye This relationship was not constant, some normal animals giving definite evidence of retention and others with extensive gross and microscopic lesions giving essentially normal responses It was concluded that although the test, in itself, is not a reliable index of the extent of pathologic changes in the liver or of the presence of impairment of other functions of that organ, it may indicate hepatic injury, and is perhaps as valuable in this connection as any procedure in use at the present time

3 In view of the several uncontrollable factors that are concerned in the metabolism of carbohydrates, it would seem that the utilization of any phase of carbohydrate metabolism in the measurement of hepatic functional activity is almost hopeless. All of the author's investigations in this connection tend to confirm this pessimistic viewpoint.

4. Tests based upon the rôle of the liver in protein metabolism and upon its so-called "detoxifying functions" have thus far failed to yield results which justify their employment as a means of quantitating the extent of hepatic injury



5. These studies indicate that extreme caution must be exercised in attempting to postulate the nature or extent of morphologic changes in the liver on the basis of so-called tests of hepatic function. Whereas "several of these tests may be of value clinically, it would seem that unless their use is combined with other methods of determining hepatic disease, they may cause serious error."

In recent years, several investigators have emphasized the significance of hypocholesteremia and diminution in the cholesterol ester fraction of the blood plasma in the diagnosis of intrahepatic disease. In a recent experimental investigation of this subject, W. B. Hawkins and A. Wright (J. Exper. Med. 59:427 (Apr.) 1934) found that the hypercholesteremia of chronic biliary obstruction was promptly reduced below normal by chloroform poisoning or bile duct infection. It was also noted that whereas acute hepatic injury due to chloroform anesthesia at times caused no change in plasma cholesterol, chronic cholesterol intoxication produced hypocholesteremia with dissociation of the normal ratio of esterified to total cholesterol, *i. e.*, diminution in the plasma cholesterol ester fraction. The authors state, "It is important to emphasize the significance of the ratio of esterified to total cholesterol as a criterion of impairment of liver function over any change that may occur in the total plasma cholesterol. The normal maximum variation which may occur in the total plasma cholesterol is very wide but the ratio of esterified to total plasma cholesterol is more constant (from 40 to 70 per cent). The constancy with which this ratio is maintained in dietary extremes and disturbed liver function indicates a physiological process capable of great compensatory effort. When values for the ratio of cholesterol esters of the plasma fall below the 'low normal' it is an indication of impairment of the functional capacity of the liver."

In a study of 512 cases of calculous and noncalculous cholecystitis, A. Cantarow (Arch. Int. Med. 54: 540 (Oct.) 1934) emphasized the importance of the routine investigation of hepatic functional efficiency before operation in such cases. The results of this study may be summarized as follows:

1. In a group of 49 patients with acute cholecystitis, hyperbilirubinemia was present at some time in 8 cases, bromsulphalein retention in 11, hypercholesteremia in 2, hypocholesteremia in 4, and urobilinuria in 4

2 Evidence suggestive of hepatic functional impairment was noted in 76 (26.3 per cent) of 288 patients with chronic noncalculous cholecystitis. Retention of bromsulphalein without hyperbilirubinemia was noted in 32 cases, hyperbilirubinemia and dye retention in 29, and hyperbilirubinemia without dye retention in 15. Hypercholesteremia was present in 4 cases, hypocholesteremia in 15, and urobilinuria in 16.

3 Evidence suggestive of hepatic functional impairment was obtained in 61 (44.8 per cent) of 138 patients with calculous cholecystitis. Dye retention was present in 52 cases, hyperbilirubinemia in 50, hypercholesteremia in 7, hypocholesteremia in 15, and urobilinuria in 15.

4 Abnormal findings were obtained in 31 (83.7 per cent.) of 37 patients with stone in the common duct

The following points were emphasized on the basis of the data presented.

(1) That some evidence of disturbed hepatic function may be obtained in a fairly large proportion of cases of calculous and noncalculous cholecystitis.

(2) That marked grades of bromsulphalein retention, even to 100 per cent., may occur in patients with disease of the biliary tract in the absence of hyperbilirubinemia.

(3) That in certain cases of stone in the common duct, some degree of dye retention persists for a variable period after a previously high serum bilirubin concentration has returned to normal

**Plasma (Serum) Phosphatase in Jaundice.**—W. M. Roberts (Brit. M. J. 1:734 (Apr.) 1933) was one of the first to record the observation of a rather marked increase in the phosphatase activity of the blood serum of patients with jaundice. In a report of 50 cases he stated his belief that this phenomenon occurred to a marked degree only in obstructive jaundice and suggested the possibility of differentiating this from other types of jaundice on this basis. This possibility has not been substantiated by more recent studies. A. Bodansky and H. L. Jaffe (Proc. Soc. Exper. Biol. and Med. 31:107 (Oct.) 1933) found a striking increase in serum phosphatase activity in a large series of patients with catarrhal icterus and hepatitis. Employing a method which is outlined elsewhere (p. 1000) they obtained phosphatase values of 4.8 to 23.8 units (adult normal 1.5 to 4 units) with icterus index values ranging from normal to 58. With subsidence of the jaundice, the phosphatase values diminished approximately in proportion to the drop in the icterus index. In a later study, the same authors (*Ibid.* 31:1179 (June) 1934) observed an increase in serum phosphatase of from 4 to 320 units in dogs with experimentally produced obstructive jaundice, the serum bilirubin concentration ranging from 3.1 to 7.9 mg. per 100 c.c. The disproportion between the phosphatase and bilirubin values in experimental animals suggests that these two factors are not interdependent.

C. H. Greene, H. F. Shattuck and L. Kaplowitz (J. Clin. Investigation 13:1079 (Nov.) 1934) reported high phosphatase values in patients with obstructive jaundice, hepatitis and portal cirrhosis and the previously noted findings in obstructive jaundice were also corroborated by the observations of A. R. Armstrong, F. J. King and R. I. Harris (Canad. M. A. J. 31:14 (July) 1934). The latter also reported the results of their studies in 19 dogs following ligation of the common bile duct. The serum phosphatase in every case rose to progressively higher values each day, reaching 30 to 100 times the initial amount after 6 days. In 2 cases in which the obstruction was later relieved, the recovery phase was accompanied by a fall in the serum phosphatase to the initial level. No appreciable rise was observed in 3 cases of experimentally produced hemolytic jaundice in dogs and in 2 cases of latent hemolytic jaundice in humans. In a group of animals with hepatic functional impairment produced by various combinations of Eck-fistula, high voltage x-ray irradiation and carbon tetrachloride intoxication, F. W. Hartman and V. Schelling (Arch. Path. 18:594 (Oct.) 1934) noted an increase in serum phosphatase activity paralleling results obtained by cholesterol, bilirubin and bromsulphalein determinations.

**DEXTROSE TOLERANCE.**—Despite their wide clinical application, there is considerable difference of opinion regarding the reliability of dextrose tolerance tests in the diagnosis of diabetes mellitus. The majority of authorities are careful to emphasize the difficulty of properly evaluating the results obtained by this method, a difficulty which is enhanced by the multiplicity of laboratory procedures employed in the performance of the test. According to W. G. Exton and A. R. Rose (Am. J. Clin. Path. 4:381 (Sept.) 1934) the chief factors responsible for the variable results are: (1) the time taken to make the test; (2) the antecedent diet or food habits of the subject; and (3) the rate of absorption of ingested glucose from the stomach. The first two factors have been sufficiently emphasized and their importance is generally recognized. In most laboratories the commonly accepted practice is to give 100 Gm. of glucose in 250 c.c. of water or  $1\frac{3}{4}$  Gm. per kilogram of body weight in about a 40 per cent. solution. Previous studies have shown that there is an extremely wide degree of variation in the rate of passage of glucose from the stomach into the duodenum when given in such concentrated solution, with consequent changes in some phase of the postabsorptive blood sugar curve. E. J. Magers (J. Lab. and Clin. Med. 19:608 (Mar.) 1934) found practically identical blood sugar responses following the administration of 50 Gm. of glucose in 15 per cent solution when taken by mouth and when administered intraduodenally.

Many observers have demonstrated clinically and experimentally the fact that normal individuals react to repeated doses of glucose with either hypoglycemia or little or no change in glycemia, while diabetics react with definite hyperglycemia. This has been explained on the basis that the first dose of glucose stimulates the insulin-glycogen mechanism to such activity that the normal organism is subsequently able to deal with added amounts of glucose without becoming hyperglycemic. Diabetics react with distinct hyperglycemia because of deficiency in the insulin-glycogen mechanism.

These principles have been embodied by Exton and Rose in what they term the 1-hour, 2-dose glucose tolerance test, performed as follows:

Dissolve 100 Gm. of glucose in 650 c.c. of water, flavor with lemon and divide into 2 equal portions (50 Gm. in 15 per cent solution). The following steps are taken in the morning, nothing having been eaten after the previous evening's meal:

1. Collect blood and urine (A) specimens, give the first dose of glucose
2. Thirty minutes later collect blood sample (B) and give the second dose of glucose
3. Thirty minutes later collect blood and urine samples (C)

The criteria of a normal response are as follows: (1) Fasting blood sugar within normal limits, (2) a rise in blood sugar not exceeding 75 mg. in the 30-minute sample, (3) the blood sugar in the 60-minute sample is less than, the same as, or does not exceed the 30-minute sample by more than 5 mg., and (4) all urine specimens are negative to Benedict's test.

The criteria for determining *diabetes* by this procedure are a more or less steep rise of not less than 10 mg. of blood sugar in the 60-minute sample following the second dose of glucose and the relation of the blood and urine sugar values to the severity of the disease.

The criteria of *alimentary glycosuria* are a sugar-free urine after fasting, with sugar in the final urine and blood sugars that follow the normal curve even when the level is higher than normal.

The authors believe that apart from its greater convenience, all available evidence indicates that the results obtained by this procedure are more specific and reliable than those obtained by previous methods.

**The Liver and Dextrose Tolerance.**—As stated above, there is considerable doubt as to the specificity of the dextrose tolerance test in indicating the presence of a defective insulin-glycogen mechanism. Recent studies by S. Soskin, M. D. Allweiss and D. J. Cohn (*Am. J. Physiol.* 109: 155 (July) 1934) cast still more doubt upon the importance of the pancreatic islet secretion in directly determining the postabsorptive blood sugar curve. These authors maintained a constant blood sugar level in depancreatized dogs by introducing a steady supply of insulin. If the response of the pancreas were a major factor in determining the normal tolerance curve, the administration of glucose to such animals should result in abnormal curves, since no additional supply of insulin was available for mobilization. It was found, however, that the blood sugar curves obtained under these conditions were essentially normal. These findings strongly suggest that the pancreas is not essential to the metabolic reactions which determine the normal dextrose tolerance curve. Experiments upon hepatectomized dogs receiving a constant supply of glucose indicated that the presence of the normal liver is essential to the normal dextrose tolerance curve and that, when the liver is absent, the intact pancreas and musculature are unable to produce a normal response. Subsequent studies by S. Soskin and M. D. Allweiss (*Ibid.* 110: 4 (Nov.) 1934) of the hypoglycemic phase of the dextrose tolerance curve, conducted upon depancreatized dogs receiving a constant supply of glucose and insulin, substantiated the belief that the normal curve is dependent upon factors residing in the liver rather than in the pancreas.

These extremely important findings, while they do not entirely discredit the present clinical interpretations of abnormal blood sugar curves following the ingestion of glucose, cast considerable doubt upon the validity of the widespread belief in the fundamental importance of the pancreas in this connection.

# THERAPEUTICS, GENERAL

*by*

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**THERAPEUTICS.**—The physician of today is accepting too freely the therapeutic suggestions which are furnished to him by the various manufacturing houses. He is failing to give due thought to the pharmacology involved. Insufficient, if any, reports of animal experimentation accompany the ideas presented. These new drugs are intended to take the place of drugs which are tried and true, have withstood the test of time clinically, and have proven themselves to be nontoxic, or their toxic dose and manifestations are well known. This is particularly true in reference to the hypnotics and is serious because of the great number of tragedies from their use which are accumulating in the medical literature. Greater thought and case reports of unusual actions or results from the U. S. P. drugs would be of great benefit to the profession. Expense is always a factor. Why use a new, expensive compound when equally as good or better results may be obtained by a U. S. P. or N. F. drug, *i. e.*, cod-liver oil in rickets, according to De Saicetes and Craig, has proved to be of greater efficiency than any of the newer products recommended. The use of chemical or expressive names for a preparation would be of assistance instead of the various proprietary names with which manufacturers label their products.

**ACETARSONE.**—*Administration and Dose.*—The use of this remedy administered by mouth in the treatment of 54 cases of *congenital syphilis*, is reported by A. S. Traisman (Am. J. Dis. Child. 46:1027 (Nov.) 1933). Dosage used: First week, 0.005 Gm. ( $\frac{1}{12}$  grain) per kilogram ( $2\frac{1}{5}$  lbs.) of body weight administered daily, the second week, 0.01 Gm. ( $\frac{1}{6}$  grain); the third week, 0.015 Gm. ( $\frac{1}{4}$  grain); and the fourth week, 0.02 Gm. ( $\frac{1}{3}$  grain). During the following 5 weeks the dosage was 0.02 Gm. ( $\frac{1}{3}$  grain). The drug was dissolved in water and given  $\frac{1}{2}$  hour before feedings. In infants under 1 year, 71 per cent showed a reversal of the Wassermann and Kahn reactions. Between 1 and 6 years of age, the Wassermann reaction became negative in 55 per cent, and the Kahn in 33 per cent. Between 6 and 12 years of age, the Wassermann reaction became negative in 47 per cent, and the Kahn reaction in 19 per cent. The clinical symptoms improved rapidly and the physical development also showed marked improvement.

No serious urinary changes were noted, except in one child who developed a severe arsenical dermatitis and died on the seventeenth day after the onset of symptoms. Associated anemia of the blood improved rapidly. Lesions of the bones showed rapid healing in all cases, both clinically and roentgenologically, after one course of treatment.

J. F. Coppolino (*Ibid.* 47:272 (Aug.) 1934) reports similar results and concludes that acetarsonic is extremely effective for young infants, rendering them symptom-free and changing the serologic reactions to negative; it is not so efficacious, however, in the treatment of older children, being more useful in causing clinical improvement than in reversing the serum reaction.

F. Eckardt (Jahrb. f. Kinderh. 141:278, 1934) administered 12 to 15 Gm (3 to  $3\frac{3}{4}$  drams) of acetarsonic in the course of about 12 weeks, which was generally adequate. As a rule, periods of 4, 6 and later 10 days of medication

were followed by pauses of 4 days. With a gradual increase of dose, treatment is continued for 12 weeks, when it is stopped, followed by a rest period of 4 weeks; it may then be repeated. There is surprising improvement of the general condition and gain in weight. The coryza often persists for longer periods and in the severe forms of visceral syphilis, acetarsone is generally no more effective than other antisyphilitic remedies. Eckardt concludes that the high percentage of effectiveness of acetarsone and the simple oral application make it the method of choice in the treatment of congenital syphilis.

**ACETYSALICYLIC ACID.**—*Untoward Effects.*—The action of acetylsalicylic acid on unstriated muscle is decidedly excitant as shown by its toxic manifestations such as, angioneurotic edema, urticaria, vasomotor spasm, spasm of the glottis, etc. The toxic dose varies greatly with the individual.

Three cases of what amounts to an idiosyncrasy are reported by A. K. Roy (Nova Scotia Med. Bull. 13:76, 1934). All of the patients had taken  $6\frac{1}{2}$  grains (0.42 Gm.) of the drug; in 20 minutes, a queer sensation followed, and in 3 to 12 hours, urticaria appeared on the neck and chest; there was also marked edema of face and hands which persisted for 3 days, then gradually disappeared.

C. Shookhoff and D. L. Lieberman (J. Allergy 4:506 (Sept.) 1933) report 3 cases of hypersensitiveness to acetylsalicylic acid expressed by a syndrome of angina pectoris, accompanied in 2 cases by urticaria. None of the characteristic signs of myomalacia were present. One thoroughly studied case showed definite allergic manifestations and definite electrocardiographic change during the attack. The electrocardiographic changes disappeared before the subsidence of the reaction. This syndrome was produced in the patient with every administration of the drug and was controlled to some degree by the administration of epinephrine. There were evidences of preexisting cardiovascular disease in all 3 of these patients.

Because of the possibility of the catastrophe which occurs in an acetylsalicylic sensitive person and because they rarely give positive skin reactions, W. W. Duke (*Ibid.* 4:426 (July) 1933) suggests the following *test for sensitivity in allergic patients*, i. e., the breaking of several fragments from a tablet of acetylsalicylic acid, placing one fragment on the patient's tongue and having him move it around his mouth. A violent attack of cough, asthma, and itching may be precipitated in 1 minute. The attack can be stopped within a minute or two by having the patient rinse his mouth repeatedly with a solution containing 4 c.c. (1 dram) of dilute acetic acid to a glass of water. Acetylsalicylic acid is insoluble in water and in dilute acids and is soluble in alkaline media, such as the saliva.

**ACRIFLAVINE.**—*Therapeutics.*—The routine treatment of gonorrhea by R. P. Herrold (J. A. M. A. 103:1821 (Dec. 15) 1934) consisted of a daily anterior in and out injection of 1:4000 dilution of acriflavine hydrochloride. The treatment is given with the patient on the table. The urethral content is released slowly and the cotton is applied over the meatus in the upright position. The use of 2 to 4 c.c. ( $\frac{1}{2}$  to 1 dram) with but momentary retention makes it unlikely that any antiseptic is forced into the posterior urethra. After 2 to 3 weeks of daily treatment, dilute to 1:6000 or 1:8000 solution. He concludes



that one daily application of an antiseptic is sufficient to control mild infections and is safer than frequent injections.

Severe infections are not suitable for local application of antiseptics, and borderline infections should have local treatment, discontinued if clinical improvement is not prompt.

**ALCOHOL.—*Untoward Effects.***—Many physicians have frequently emphasized the rôle which *alcoholism plays in the fatalities from pneumonia*. Harlow Brooks (J. A. M. A 103:1192 (Oct. 20) 1934), in a review of 200 fatal cases of pneumonia with autopsy, shows that in only 5 instances was alcoholism a factor. He expresses the opinion that this factor in pneumonia fatalities has been overestimated, but states he feels that chronic alcoholism, with its attendant exposure and other concurrent factors, at least looms large as an important factor in susceptibility.

***Therapeutics.***—W. M. Wilson (Northwest Med. 33:268 (Aug.) 1934) advocates the use of 95 per cent. alcohol in the treatment of *chronic vulvitis* and *pruritus vulvæ*. The details of technic of treatment are given as follows:

Stone's method for the injection of alcohol in pruritus ani has been applied successfully in the treatment of pruritus vulvæ. With the patient in the lithotomy position, the vulva is as carefully prepared as it would be for surgery, except that shaving is probably not necessary. The vulval structures are then examined to determine the exact location and extent of the itching for each part. The patient will usually point to areas of the most intense itching and neglect to make any reference to parts less involved.

The patient should be then anesthetized, preferably with a general anesthetic. The alcohol is injected by means of an ordinary 2 c c hypodermic syringe which should be calibrated in minims. The needle is inserted perpendicularly to and through the skin so that the alcohol will be deposited just beneath the dermis. An injection into the skin itself or too deeply into the subcutaneous tissues is apt to produce a slough. Only 3 or 4 minims (0.2 or 0.24 c c) of alcohol are injected at a single insertion of the needle. The number of injections for any one structure or area depends upon the extent of the itching, the age of the patient, and the condition of the peripheral circulation as well as the estimated efficiency of the circulation of the part to be injected.

Generally speaking, elderly patients with arteriosclerosis or vulval and anal varicosities should be injected cautiously. When the skin is in fair condition and the circulation seems unimpaired, as much as 4 minims (0.24 c c) of alcohol may be injected into every sq. cm. of the itching area. The best results have been obtained in cases where the itching areas were most thoroughly injected. When, however, the skin is much thickened or excoriated, or the circulation seems impaired, the injections must be made at wider intervals and only 2 or 3 minims (0.12 or 0.2 c c) injected at one insertion of the needle.

Almost immediately after injection, the vulval folds, particularly the labia majora, become more or less edematous. The edema increases for from 12 to 24 hours and then subsides slowly for several days. At the end of this time the labia majora are still sometimes a little tender to firm pressure or manipulation.

The itching usually stops immediately, or within 24 hours, though occasionally 1 or 2 small areas of itching remain. These are usually small areas that were overlooked. The subcutaneous induration subsides in from 4 to 8 weeks.

*Complications* developed in one patient, a small *hematoma* appearing in the left labium majus during injection, which required incision and drainage 11 days later. Edema impaired the vulval circulation and resulted in a *slough* in the left labium majus, which required incision and drainage after 10 days. The wound healed without complications or discomfort.

Other changes observed following alcohol injection were skin lesions of the vulva, including excoriations, cracks, fissures, dermatitis, folliculitis and furunculosis, which heal promptly and disappear in from 3 to 10 days. The grayish discoloration of the skin gradually disappears so that skin coloration from 6 to 8 weeks after injection is normal. In every case where the skin was indurated or thickened and had lost much of its elasticity alcohol injections effected an immediate softening and partial or complete return of its elasticity.

In *leukoplakic vulvitis* the appearance of the vulva changed rapidly following injection. Most of the visible leukoplakia disappeared in from 10 to 20 days. Pruritus recurred in 3 cases, but only a few patches of leukoplakia have been seen. Biopsies before and 40 days after treatment showed that much of the leukoplakia and practically all signs of inflammation of the vulval skin had disappeared.

Alcohol is being more widely used in France for *pulmonary suppurations* since the technic of the method has been perfected. Already, manifest results have been secured (J. A. M. A 102: 1241 (Apr 14) 1934).

E. Merle and Gurfinkel (Bull. et mém. Soc. méd. d. hôp. de Paris 49: 1614 (Dec 25) 1933) reported excellent results in 3 cases of pulmonary suppuration and state that these observations justify the use of intravenous alcohol as a method of the first order in the treatment of acute or chronic pulmonary suppurations when surgical treatment (*a*) is not yet indicated, (*b*) when its indications are doubtful, (*c*) when it is no longer possible. The harmlessness of this treatment, already established by various authors, appears absolutely certain to Merle and Gurfinkel. In more than 250 injections they observed no serious untoward incidents aside from the regularly occurring pain symptoms and signs of shock (commonly moderate). They conclude that this shock could be ascribed to the strong hemolytic action of the solutions in the serum + 5 per cent dextrose or in the artificial serum. The optimal dose of this solution appears to be from 40 to 50 c.c. ( $1\frac{1}{3}$  to  $1\frac{2}{3}$  ounces) per injection. In order, however, to secure therapeutic results, it appears indispensable to use rather large total doses, thus necessitating for a cure a total quantity of from 200 to 300 c.c. ( $6\frac{2}{3}$  to 10 ounces) of 45 per cent alcohol, or from 600 to 900 c.c. (20 to 30 ounces) of the 33 $\frac{1}{3}$  per cent solution.

Z. Brull (Med. Klin. 30: 576 (Apr 27) 1934) successfully employed alcohol in various *pulmonary* conditions such as *abscess*, *gangrene*, *lobar pneumonia*, *bronchopneumonia* and *bronchiectasis*. He administered 15 per cent alcohol in distilled water in doses of 20, 25, 30, 35, or 50 c.c. ( $\frac{2}{3}$ ,  $\frac{5}{6}$ , 1,  $1\frac{1}{6}$ , or  $1\frac{2}{3}$  ounces). In contradistinction to the more concentrated alcoholic solutions, the 15 per cent

solution proved entirely harmless and was well tolerated by the vein. As a result of this injection treatment, 8 patients with acute solitary pulmonary abscesses and gangrene recovered without operation. The alcohol injections produced a considerable improvement in 3 of 8 patients with bronchiectasis. Six of 8 patients with bronchopneumonia were greatly improved by the alcohol injection. In 5 cases of lobar pneumonia, the alcohol injections exerted a favorable effect, but did not shorten the course of the disease. In pulmonary tuberculosis the alcohol injections were ineffective.

It was found by R. Grasso (Policlinico 41:526 (Oct.) 1934) that complications could be prevented when intravenous injections of alcohol were administered in large doses to healthy animals exposed to pulmonary complications through artificially-produced anatomic conditions (simple tracheal fistula with the introduction of microorganisms into the bronchial tree). Treatment was insufficient, when, because of the tracheo-esophageal fistula, the pulmonary infection was more serious and involved. He cites 4 cases presenting gangrenous pulmonary abscess in which daily intravenous injections of 2 c.c. ( $\frac{1}{2}$  dram) of 33 per cent. solution of alcohol were administered. No favorable results were obtained. The injections did not succeed in checking the progressive course of the disease or in influencing the expectoration and temperature. He believes that his negative results are not sufficient to disprove the efficacy of alcohol therapy in pulmonary diseases, if administered in the early stages and in sufficient dose.

**ALUMINUM HYDROXIDE.**—*Therapeutics.*—The use of aluminum hydroxide is advocated by I. H. Emsel, Lloyd Adams and Victor C. Myers (Am J Digest Dis and Nutrition 1:513 (Sept.) 1934) in the treatment of *peptic ulcer*. They observed that a number of patients became symptom-free in from 2 to 7 days, even if they had had a recurrence lasting for several months. The 110 patients were treated from 1 month or less to 3 years. There were 9 patients in whom symptoms remained and who had recurrences. The patients were put on a modified Sippy convalescent diet, consisting of 6 feedings a day, followed by from 1 to 3 drams (4 to 12 c.c.) of gelatinous aluminum hydroxide from  $\frac{1}{2}$  to 1 hour after the ingestion of food. Constipation was controlled by agar and liquid petrolatum. Phenolphthalein was added when necessary. The patients after the first 2 or 3 weeks were allowed to work, if this was not too strenuous. The free acidity of the stomach is lowered after treatment with aluminum hydroxide but returns to the initial level after the medication is discontinued. Although aluminum hydroxide serves obviously as a gastric antacid, it is possible that its efficacy in the treatment of peptic ulcer may be dependent, in part at least, on its slight astringent and demulcent properties and the fact that it appears to increase the secretion of mucus. No contraindications for aluminum hydroxide therapy have been observed.

**AMIDOPYRINE.**—*Untoward Effects.*—The literature for the year has been abundant in reports on the harmful results of amidopyrine, particularly as a possible cause of leukopenia states.

It is suggested by L. F. Herz (J Lab and Clin Med 20:19 (Oct.) 1934) that the drug should be strictly banned by the medical profession because of its

dangerous character. When anodynes or antipyretics are indicated, acetanilid is a safe drug which should be given in therapeutic doses best combined with caffeine and sodium citrate. An alternative, but less efficient drug, would be acetphenetidin. By using the safer antipyretics, there is no doubt that greater efficiency will be obtained and granulocytopenia and other toxic phenomena now known to be caused by the dangerous pyrazolon group of drugs (amidopyrine and antipyrine) will be eliminated.

**Therapeutics.**—Despite all the adverse criticism of amidopyrine, G. Petranyi (Am. J. Dis. Child. 46:1011 (Nov.) 1933) claims that in the treatment of *grip* in children, medicine administered was most effective (1) when it contained amidopyrine or its derivatives, (2) when doses larger than usual for babies and young children were given. He administered amidopyrine in unadulterated form in the following dosage, day and night, until the temperature reached normal from birth to 1 month of age, 0.05 Gm ( $\frac{5}{100}$  grain); from 3 to 6 months, 0.1 Gm ( $\frac{1}{10}$  grains), from 6 to 12 months, 0.15 Gm. ( $\frac{3}{20}$  grains), and from 2 to 5 years, 0.2 Gm (3 grains). As soon as the temperature had fallen below 98.6° F. (37.0° C.) and had remained at this point for at least half a day, the intervals between the doses were lengthened to 3 hours, and if fever did not recur in 4 hours, it was sufficient to administer the amidopyrine only 3 times a day. The amidopyrine was prescribed in a 3 or 4 per cent solution, to be taken in concentrated syrup. To stop the medicine too soon or too suddenly is an error, for the diminishing of the concentration of amidopyrine demands great care, as otherwise the drug does not have its full effect. In the treatment of 100 cases, the most satisfactory results were obtained from patients who showed sudden and severe symptoms, high fever and occasional delirium. In these patients, after the introduction of the treatment, the fever generally diminished gradually in from 12 to 24 hours, in most cases the great exhaustion and weakness as well as the occasional delirium were checked. Most of the best results are obtained in cases in which treatment is given immediately.

**AMNIOTIN.**—**Therapeutics.**—J. Huberman and H. H. Israeloff (J. A. M. A. 103:18 (July 7) 1934) investigated on ambulatory patients the use of amniotin in the treatment of *juvenile gonorrheal vaginitis*. In 6 cases, 100 rat units of hypodermic amniotin was administered 3 times a week. The children of this group, including 3 old cases, were clinically cured after receiving a total average of 21 injections. No other form of treatment was employed. No local or constitutional reactions were manifested. The vaginal smears were negative for gonococci at the end of 4 weeks.

In the second group he used 3 acute cases. In this series the vaginal discharge disappeared in 8 weeks and required an average of 27 injections. Regardless of the amount of amniotin administered, no hypertrophy of the breasts or labia, or any internal bleeding was observed. One case was given larger doses by mouth, with similar results. (This would prove of particular value in the eradication of the disease if it should prove to be permanent.)

**ANESTHESIA.**—In the pharmacologic evaluation of new chemicals for various uses in anesthesia, as elsewhere, the essential factor is the critical quantitative estimation of the ratio of the toxicity of the substance to its efficiency, in comparison with related agents. Both the toxicity and the efficiency must be thoroughly investigated. If the toxic dose range overlaps the effective dose range, the drug is not safe. The drug that has the greatest margin of safety between the effective dose and the toxic dose will in general be best. Too seldom are full data on this essential matter in anesthesia given to physicians.

**ETHYLENE.**—As an anesthetic this has not been used nearly so frequently as its merits would justify. Exaggerated accounts of explosions have caused such unwarranted fears that the mind of man is still prejudiced. Isabelle C. Herb has published an account of over one million ethylene anesthetics with no explosions and no deaths. W. Bourne (Canad. M. A. J. 31:44 (July) 1934) states that ethylene anesthesia is more easily maintained than that of nitrous oxide, more oxygen may be given, there is better muscular relaxation, the vital functions are not depressed to any greater extent, and recovery is just as early, with little or no vomiting, and with the ability to clear the throat.

In practice it will be found that when it is advisable to mix ether vapor with ethylene, relatively very little will be necessary and that toward the end of the operation the *ill effect of ether* may be alleviated by washing it out with an abundance of a mixture of **oxygen** and **carbon dioxide**.

**CYCLOPROPANE** ( $\text{CH}_2$ ,  $\text{CH}_2$ ,  $\text{CH}_2$ ).—This new gas promises to be more valuable than ethylene. J. A. Stiles, W. B. Neff, E. A. Rovenstine and R. M. Waters (Anesth. and Analg. 13:56 (Mar.-Apr.) 1934) have shown its usefulness to man.

The gas is more potent than either nitrous oxide or ethylene, 18 per cent. being sufficient to produce profound anesthesia.

As an anesthetic it produces greater muscular relaxation than the other gases. It is reported from the Universities of Toronto and Wisconsin that the pharmacological effects of cyclopropane and oxygen are such that anesthesia is produced without the metabolic disturbances which are caused by other anesthetic agents.

W. Bourne and B. B. Raginsky have demonstrated that cyclopropane does not impair liver function nor enhance the damage deliberately produced with chloroform. Bourne believes it will be of great aid in *obstetrics*. He has already produced intermittent analgesia as well as continuous anesthesia during parturition.

The basis of expectation of the usefulness of cyclopropane is so high that its present prohibitive cost will be considerably reduced.

**DIVINYL OXIDE.**—A new ether divinyl oxide ( $\text{CH}-\text{CH}(\text{O})-\text{CH}=\text{CH}_2$ ) has been introduced by C. D. Leake (J. A. M. A. 102:1 (Jan. 6) 1934). Pure divinyl oxide, although explosive, like ether and ethylene, is more powerful and rapid in its anesthetic action. It is more volatile than ether (boiling point  $28.3^\circ \text{C}$ ) and less irritating locally. Its minimal certain anesthetic concentration is shown when allowed to act for 10 minutes, but greater circulatory reserve remains when respiration fails. Recovery is more prompt than from ether or

ethylene and less attended with nausea. Relaxation without intercostal muscle paralysis may more easily be obtained with divinyl oxide than with more common general anesthetics.

Divinyl oxide is not an ideal anesthetic. In addition to its explosibility and probable expense, it may polymerize or decompose with the appearance of such dangerous irritants as paraldehyde and formic acid.

S. Goldschmidt, I. S. Ravdin, B. Lucke, G. P. Muller, C. G. Johnston, and W. L. Ruigh (*Ibid.*, p. 21) report on 461 cases of anesthesia with divinyl ether, 90 per cent. of which were given by the open drop method. The first stage is short. Consciousness is lost after a few inhalations. They conclude from their observations that from the standpoint of induction, maintenance, and recovery, the anesthetic is satisfactory. It affords rapid surgical anesthesia with a minimum amount of the anesthetic, even maintenance, good relaxation, and rapid recovery. No untoward effects have been observed on the blood-pressure or respiration. The very low incidence of excitement or postanesthetic vomiting and of respiratory complications is noteworthy. The anesthetic should be carefully administered, since the lethal concentration of divinyl ether in the dog is only about one-half of the anesthetic concentration of diethyl ether (ether). The circulation is well maintained for a time after cessation of respiration.

In the human being they have encountered no untoward effects on the liver or kidneys. Divinyl ether failed to produce liver necrosis in the monkey under any of the conditions imposed on it.

**ETHER.**—Widely divergent opinions prevail as to the effect on patients of ether taken from a container that has been opened any length of time. Some state that it becomes very toxic and irritant. H. Gold and D. Gold (*J. A. M. A.* 102:817 (Mar. 17) 1934) conclude, as a result of a series of tests, as follows:

1. U. S. P. ether in metal cans, as it is supplied in this country at the present time by the better known manufacturers, does not deteriorate rapidly under ordinary conditions when the metal containers are opened. The present study shows that the can may be opened and again stoppered with cork many times during periods of weeks without oxidation detectable by the U. S. P. tests.

2. There is no evidence that ether especially purified "for anesthesia" has any material advantage over ordinary U. S. P. ether for anesthetic purposes.

3. It is recommended that hospitals buy ordinary U. S. P. ether in large steel drums and that for anesthesia the operating rooms be supplied with ether in small tin cans filled daily from the drums by the hospital pharmacist. The ether in the drum may be tested daily for aldehydes and peroxides, there being very simple tests for each, requiring only from 5 to 10 minutes to perform. This would help not only to correct an erroneous view regarding the speed of deterioration of ether after the container is opened, but to abolish the extravagant practice of buying ether in hundreds of quarter-pound or half-pound cans at from 4 to 6 times the cost of ether in drums, when large quantities of ether for anesthesia are used.

. Current interest in preanesthetic hypnotics is focused on the barbiturates, to the unfortunate neglect of many other equally promising chemical types. The "success" of tribrom-ethanol as a "basal anesthetic" is chiefly commercial, phar-

macologic and clinical evidence failing as yet to indicate that it is any better than paraldehyde by rectum.

**TRIBROM-ETHANOL.**—A. Schulte (Zentralbl. f. Gynäk. 57: 2565 (Oct. 28) 1933) employed tribrom-ethanol in 1216 gynecologic operations. He lists the various usual types of operations and states that in over 50 per cent. of the cases tribrom-ethanol anesthesia effected a complete or nearly complete anesthesia, while in the others some ether had to be given. In slight *complications* that may arise, **oxygen inhalation** is generally sufficient, but cardiac stimulants should be at hand and the blood-pressure should be controlled. It failed completely in 8 cases. Three patients died during or after the operation, but these fatalities were probably caused by the extreme weakened condition of the patients rather than by the anesthetic. Schulte's general conclusion is that tribrom-ethanol anesthesia compares favorably with other types. He stresses as its main advantages the simplicity of its application, the elimination of the period of excitation, the complete retrograde amnesia and the absence of postoperative pulmonary complications.

**Anesthesia.**—Bourne claims that tolerance to tribrom-ethanol does not develop and consequently the same dose may be used on different occasions with approximately equal effects. E. E. Arnheim and L. R. Tuchman (Arch Surg. 29: 1 (July) 1934) studied the effects of tribrom-ethanol of 15 normal individuals in order to ascertain the uncomplicated effects of the drug. They found

- 1 Increase in the pulse rate, average increase of 16 per minute.
- 2 Increase in respiratory rate, average increase, 6 per minute
- 3 Decrease in amplitude of respiration
- 4 Average increase of 1.3° F in rectal temperature
- 5 Average decrease in systolic blood-pressure of 24 mm
- 6 Average decrease in basal metabolism of 22 per cent
- 7 Average decrease in clotting time of 3 minutes
- 8 Slight rise of blood sugar, slight fall of carbon dioxide content of the blood and a slight rise of plasma volume
- 9 Negligible change in a venous pressure, blood cholesterol and cholesterol ester, blood calcium, blood chlorides, and formed blood elements
- 10 Slight oliguria and an increase in the specific gravity of the urine
- 11 Loss of conjunctival and tendon reflexes, with a late preservation of cutaneous and pharyngeal reflexes
- 12 Slight cyanosis in 2 instances, increase in the secretion of mucus in the pharynx in 5 minutes, and slight vomiting in 3 instances
- 13 No untoward effect followed the use of tribrom-ethanol in the dosage employed in basal anesthesia

**COMPLICATIONS.**—**Asphyxia.**—P. J. Flagg (New York State J. Med. 34: 665 (Aug. 1) 1934) has written an excellent monograph on the *prevention* of asphyxia during anesthesia and concludes that this turns upon the control of 2 factors, *i. e.*, the physical and the biochemical. The physical or mechanical occurs above and below the glottis. The various causes of obstruction above the glottis are well recognized. Those below the glottis are not so well understood. The biochemical causes of asphyxiation are frequently lost sight of altogether.

It is pointed out that the most accurate measurement of the anesthetic is promptly removed in the face of obstructive complications. It is also pointed out

that true asphyxia may also occur without cyanosis in the absence of adequate  $\text{CO}_2$ , in accordance with the effect described by Bohr. A brief reference to the effect of the hydrogen ion concentration upon the tidal volume of the respiration is made. The stabilizing factor is shown to be consistent maintenance of the proportion of  $\text{H}_2\text{CO}_3$  to  $\text{NaHCO}_3$  in the circulation.

The relief of asphyxiation during anesthesia is pointed out as being both chemical and physical. The *chemical control* is exercised through the **correct choice of the premedication and anesthetic agent**. The *physical* by the **correct use of the pharyngeal tube** as well as a safe and efficient **intra-tracheal inhalation tube** which should possess the qualifications of a correct diameter, widest possible lumen, combined with thinnest possible wall, intubated by direct vision.

**PREANESTHETIC MEDICATION.**—C. D. Leake (J. A. M. A. 102. 1 (Jan. 6) 1934) calls attention to a great variety of chemical adjuncts that have been proposed for (1) preanesthetic hypnosis, (2) regulation of metabolism preoperatively, (3) aid in the induction maintenance and prompt recovery from anesthesia, (4) relief of postanesthetic nausea, and (5) postoperative analgesia. It should be obvious clinically that routine preanesthetic medication or uses of chemical adjuncts to anesthesia are not for the best interests of the patient. Each patient should be individually considered with regard to the chemical to be used, if one is necessary, and to its dosage and its mode of administration. Axiomatic though this may seem, it is usually honored in the breach in anesthesia.

The objections to **morphine** are central nervous system stimulation outlasting the obvious depression, tendency to cause constipation, tendency to disturb carbohydrate and fat metabolism, depression of respiration and interference with rapidity of absorption and excretion of a volatile anesthetic. Nevertheless, it remains the best preanesthetic and postoperative analgesic when traumatic pain is present. **Codeine** is preferable, provided the traumatic pain is slight.

**Atropine** has rational indications when chloroform or ethyl chloride are to be used or when an embarrassing mucous or salivary flow is expected. Otherwise, it has little merit in anesthesia, its relaxation of the intestine probably contributing to the frequent postoperative stasis.

As a preliminary to general anesthesia, J. R. M. Whigham (Lancet 2 191 (July 28) 1934) gives 1 dram (4 c.c.) of **paraldehyde** in 12 ounces (360 c.c.) of saline solution for every 14 pounds in weight (6.4 kg.). The solution is given slowly by the rectum at body temperature, from  $1\frac{1}{2}$  to 2 hours before the operation. The patient lies on the left side with the buttocks slightly raised. The administration takes from 30 to 40 minutes. In from 25 to 45 minutes, the patient is sleeping. It has been his practice to continue anesthesia with **gas** and **oxygen** and, if necessary, a minimal amount of **ether**. When relaxation has been obtained, ether usually may be discontinued. *Deethenization* may be brought about at the end of the operation by the use of 5 or 10 per cent **carbon dioxide-oxygen inhalations**. The color of the patient is sometimes sallow after the paraldehyde has been given but improves quickly when gas and oxygen are administered and usually remains good throughout the operation.



On return to the ward, the patient recovers consciousness in from  $\frac{1}{2}$  to 2 hours. A rectal irrigation is not necessary. Postanesthetic vomiting is slight or absent. *Hiccups* occur sometimes but are well controlled by the inhalation of 5 or 10 per cent. carbon dioxide.

**ANESTHESIA IN OBSTETRICS.**—The ideal obstetric analgesic would be easily administered, would confer the maximum degree of safety to mother and child, afford a decided relief from pain, and would not interfere with the contractility of the uterine musculature. Chloroform and ether, colonic ether, morphine and scopolamine combination, nitrous oxide and oxygen combinations, all are wanting in one or more of the requirements of the ideal analgesic according to L. Averett (*Am J. Obst and Gynec.* 27: 109 (Jan) 1934).

**Penta-barbital sodium** is eliminated much more rapidly than pernocton and sodium amytal, and is, therefore, much less toxic. Penta-barbital sodium has a profound sedative but shorter hypnotic action, causes much less restlessness than sodium amytal or pernocton, and its action is readily prolonged by the addition of scopolamine. It was determined that in the average case the best results were obtained by the oral administration of 1 dose of 6 grains (0.4 Gm) of penta-barbital sodium divided into 4 capsules of  $1\frac{1}{2}$  grains (0.1 Gm) each.

**Scopolamine hydrobromide**,  $\frac{1}{100}$  grain (0.6 mg), is administered hypodermically when labor is definitely established, with satisfactory uterine contractions at least every 5 minutes, and when the cervix is partially effaced and dilated sufficiently to admit 2 fingers

In the series reported the average duration of analgesia during labor was  $5\frac{1}{2}$  hours. The dosage mentioned was used in 160 cases and only in 28 primiparas and 2 multiparas was additional medication administered, usually 3 grains (0.2 Gm) of **penta-barbital sodium** and  $\frac{1}{150}$  grain (0.45 mg) of **scopolamine hydrobromide**. The average duration of amnesia following labor was 2 hours. **Nitrous oxide** and **oxygen** was administered at the end of the second stage of labor in all cases.

The administration of the **penta-barbital sodium** produced drowsiness followed in 15 to 30 minutes by profound sleep. The respiratory rate was unchanged, in only a few cases was the pulse rate slightly increased, the blood-pressure usually dropped from 5 to 10 mm, pupils were moderately dilated, conjunctival and corneal reflexes were absent in several of the patients, nystagmus or diplopia was not observed. The frequency and severity of the uterine contractions were not interfered with. The first stage of labor was usually rapid in some cases, most likely due to the sudden relaxation and dilatation of the lower uterine segment. The second stage of labor also progressed normally. No prolongation of the third stage was noted. Postpartum hemorrhage occurred in only one case and necessitated uterine packing. Of the 160 cases studied, 126 were primiparas and 34 multiparas. The average length of labor of the primiparous patients after entering the hospital was  $9\frac{1}{2}$  hours, of the multiparous, 5 hours and 10 minutes. There was no maternal mortality in the entire series; 152 babies either breathed or cried immediately after delivery; 8 required mild resuscitation, 3 having been delivered by midforceps, and 1 was a breech presentation, with forceps used on the after-coming head.

When questioned on the day following delivery, 110 patients stated that they experienced complete amnesia after medication was administered. In 42 cases there was some recollection of a few incidents during labor, but very little recollection of pain. In only 8 patients was complete failure experienced, and these occurred in multiparas well advanced in labor upon admission and delivered in from 60 to 90 minutes after the medication.

F. G. McGuinness (Canad. M. A. J. 30:162 (Feb.) 1934) gives a report of 140 obstetrical cases in which **penta-barbital sodium** was used orally to produce amnesia. He gives a 160 lb. (72.7 kg.) patient 6 grains (0.4 Gm.) as an initial dose, a second dose of 3 grains (0.2 Gm.) not later than 3 hours, and  $1\frac{1}{2}$  grains (0.1 Gm.) every succeeding 2 hours or more if amnesia is not complete, until delivered. The drug is administered by capsules *per os*. It should be given on an empty stomach with warm water. The treatment is begun in the primipara when the os is one-third dilated and in the multipara when the os is 2 fingers dilated. The penta-barbital sodium increases the action of morphine more so than magnesium sulphate and for this reason should not be used in combination.

He concludes that with penta-barbital sodium we have (1) a simple method of relieving the pains of labor, (2) a high percentage of efficiency, with a minimum risk to the mother and no risk to the fetus; (3) little or no interference with the course of labor; (4) no increased blood loss; (5) a greatly improved convalescence.

**ANESTHETICS IN OPHTHALMOLOGY.**—E. C. Dillon and C. Greer (Arch. Ophth. 10:674 (Nov.) 1933) used **nupercaine** in 10 cases of *pterygium* by instillation and injection. None of the patients complained of severe after-pain, and in a number there was no postoperative discomfort whatever. With nupercaine a somewhat greater length of time is necessary for the induction of anesthesia, i. e., from 15 to 20 minutes in cases of *pterygium*. In some cases sufficient anesthesia could be obtained by instillation alone, while in others the injection of from 2 to 3 drops of a 1:1000 dilution was necessary. The freedom from after-pain was quite definite as compared with that in patients operated on under cocaine anesthesia. A 1:500 ointment of nupercaine was used and freedom from after-pain was noted in cases of *corneal abrasions*, *pterygium* and other conditions. Because of its prolonged anesthetic effect, nupercaine is a particularly valuable drug in certain ophthalmologic procedures.

M. K. Bochner (*Ibid.* 10:763 (Dec.) 1933) gives a summary of his experiences with nupercaine in ophthalmology over a period of 3 years. On the basis of his results he concludes that nupercaine is most satisfactory for both instillation and infiltration anesthesia in ophthalmologic practice. The maximal strength should never exceed 1 per cent. for instillation and 1:1000 for infiltration. The maximal effect does not take place for at least 10 minutes after the injection or instillation, for operations involving traction on the iris, an interval of  $\frac{1}{2}$  hour should elapse between the instillation of the first drop and the operation, unless the instillation is supplemented by a retrobulbar injection. For instillation at least from 15 to 20 drops of **epinephrine hydrochloride** per ounce (30 c.c.) should be added to overcome the vasodilator effect. The epinephrine does not

appear to increase the anesthetic action. There is only slight drying of the corneal epithelium and no alteration in the tension nor influence on the pupil results. The action is much more prolonged than that of any other anesthetic, and the drug is relatively less toxic. In more than 2000 cases, no toxic reaction was observed when the drug was used in the strength mentioned. As a nonnarcotic it lends itself readily to prescription in combination with other drugs in the form of solutions or ointments.

**SPINAL ANESTHESIA.—Overdosage.**—The following case is of interest because of the large dose of spinal anesthetic administered with a subsequent almost fatal outcome. A white woman, aged 40, weighing 160 pounds (72.7 kg.), with a systolic blood-pressure of 140 and a diastolic blood-pressure of 80, was given a spinal anesthetic for a cholecystectomy for hydrops of the gall-bladder. **Novocaine crystals** (a brand of procaine hydrochloride) dissolved in the patient's spinal fluid were injected into the third lumbar space. While the gall-bladder contents were being emptied, the patient became pulseless and stopped breathing. Cardiac and respiratory action were restored by means of subdiaphragmatic cardiac massage, epinephrine by vein and artificial respiration. The operation was terminated at this point by a cholecystostomy. The postoperative course was uneventful. It was found that the glass ampoule used did not contain the usual 120 mg. (2 grains) but contained 500 mg. (7½ grains). This ampoule was not meant for spinal use, but was used by mistake, according to Alexander Zabin (J. A. M. A. 103:507 (Aug. 18) 1934). There seems no good reason for marketing 500 mg. ampoules of novocaine.

H. G. Holder (California and West. Med. 40:95 (Feb.) 1934) uses a combination of **nupercaine** and **procaine hydrochloride** in *block anesthesia* so as to derive the advantages of both and perhaps do away with their disadvantage. In a patient properly prepared for spinal anesthesia, *i. e.*, with the administration of 50 mg. (¾ grain) of **ephedrine** in lower abdominal cases and 100 mg. (1½ grains) in upper abdominal cases, 15 minutes before lumbar puncture, the lumbar tap is made with a fine gauge needle in the second and third lumbar space, as outlined by Huff, then, 50 mg. (¾ grain) of procaine hydrochloride crystals are dissolved in 2 c.c. (½ dram) of a 1:200 solution of nupercaine. Of the 74 cases, 44 showed an average fall of systolic blood-pressure of 20.4 mm. of mercury; 14 were stabilized without fall or elevation; and 16 showed an average elevation of blood-pressure from the preanesthetic level of 23.6 mm. of mercury.

**ANTUITRIN-S.—Therapeutics.**—Anterior pituitary-like hormone obtained from pregnancy urine has established a definite place in the treatment of *undescended testes* and *infantilism*. E. T. Engle (Endocrinology 16:513 (Sept.-Oct.) 1932) suggested its use as the result of experimental indication of testicular descent in immature monkeys; following which, A. Goldman and A. Stern (New York State J. Med. 33:1095 (Sept. 15) 1933) reported the successful treatment of two boys.

D. L. Sexton (Endocrinology 18:47 (Jan.-Feb.) 1934) administered it to 13 boys with genital underdevelopment. Cryptorchidism was present in 6 of these patients, with correction in 4 of the cases. Similar results have been obtained by

S. Cohn (J. A. M. A. 103:103 (July 14) 1934) who treated 6 cases of undescended testicles with favorable results and came to the conclusion that the anterior pituitary-like principle of pregnancy urine is apparently effective in causing descent of the testes when there is no anatomic malformation acting as a mechanical obstruction, and that this hormone is a valuable adjunct to the surgical treatment of undescended testes.

S. B. D. Aberle and R. H. Jenkins (*Ibid.* 103:314 (Aug. 4) 1934) obtained complete descent in 1 of 4 cases; partial descent in another; and in 1 instance there was growth of the penis

In a case of *testicular atrophy* resulting from orchitis, W. L. Brosius and R. L. Schaffer (*Ibid.* 101:1227 (Oct. 14) 1933) injected 2 c.c. intramuscularly, twice weekly. Previous to treatment, aspermia was determined by repeated microscopic examinations. Following therapy, motile spermatozoa were observed.

An arbitrary dosage of 1 c.c. (16 minims) 3 times weekly for ten injections was employed by S. Cohn (*Ibid.* 103:103 (July 14) 1934).

**ARSENIC POISONING.—*Diagnosis.***—Frequently the symptoms of arsenic intoxication are not recognized during life because of their similarity to other disturbances, according to J. Leibowitz (Schweiz. med. Wchnschr 64:947 (Oct. 13) 1934). Even the necropsy does not always bring clarity, because the typical changes in the large organs are convincing only if the examination is made shortly after death, and even then, the changes may be mistaken for those of cholera or of certain meat poisonings. However, there remains the reliable chemical analysis. The differentiation of acute arsenic poisoning with a large dose that causes death within a comparatively short time and chronic poisoning is usually not difficult. Only a separate examination of the different organs is necessary. In *acute arsenic poisoning* (with the exception of the rare cerebral, paralytic form) death follows quickly because of the destruction of tissues in the gastrointestinal tract and before large quantities of the arsenic have reached the blood stream and other organs. In the case of *slow poisoning*, however, certain organs act as depots for the arsenic, particularly the hair, the long tubular bones, and the central nervous system. By experimenting on rabbits, the writer found that the organism of this animal eliminates most of the arsenic soon after its intake. Rabbits which died several days after the administration of the last of several doses showed a similar distribution of arsenic in the internal organs, as did rabbits that died after a single large dose. The only exception was the arsenic content of the pelt. Doses administered at long intervals did not result in a cumulative amount of arsenic in the organism. However, when 2 doses were given at short intervals, there was an accumulation of arsenic.

**ARSPHENAMINE.—*Untoward Effects.***—Six rather severe reactions to arspenamine are reported by M. Scarf (J. A. M. A. 102:2159 (June 30) 1934):

1 One case of aplastic anemia, when 2 injections were given after purpura appeared

2 Two cases of hepatitis, 1 injection of neoarsphenamine was given after the patient complained of itching.

3. Hemorrhagic encephalitis occurred as a complication in a case of gonorrheal arthritis with a negative Wassermann reaction in which 2 doses of neoarsphenamine were given in increasing doses, although an eruption followed the first dose.

4. In a case of aneurism of the aorta, rupture followed therapy which was too vigorous and not preceded by a preparatory course of the antisyphilitic drugs.

5. A case of transverse myelitis due to a rare and usually fatal form of Herxheimer reaction, terminating in a complete recovery.

The majority of these deaths could be avoided, if attention were given during arsphenamine therapy to all minor complaints of the patient in reference either to reaction of previous injection or to apparent slight disturbances, *i. e.*, itching, slight jaundice, etc. Examination of the conjunctiva should be made for early signs of icterus.

**BARBITAL.**—G. T. Gwathmey (J. A. M. A. 103:1536 (Nov. 17) 1934) considers the **sodium salt of ethylisopropyl barbituric acid** comparatively safe. He has been using it for the past 2 years as a premedication before inhalation or oil ether colonic anesthesia. He cites the case of a patient who had taken 172 grains (11.4 Gm.) of the drug. Previously she had occasionally used it for insomnia, but had not formed a habit. The 43 tablets did not seem to produce sleep more quickly than 1 tablet, and caused no unpleasantness. She regained consciousness 5 days after taking the 172 grains, following treatment as outlined by B. Fantus (*Ibid.* 103:749 (Sept. 8) 1934).

**Poisoning.**—Poisoning by barbitol, either as a result of suicide or an accidental overdose, is made the subject of frequent reports in the literature. Lately, the association of the barbiturates with amidopyrine as a cause of granulocytopenia, occurring especially in physicians and nurses and their families, is well brought out. Wm. Ravine (J. Med. 15:369 (Sept.) 1934) reports a case of chronic barbitol poisoning in a physician who had been taking barbitol preparation for 4 or 5 years in the daily dose of 3 to 6 grains (0.2 to 0.4 Gm.). No skin manifestations were present. Mental hebetude, tremor, weakness, and restlessness were the outstanding symptoms. Complete **withdrawal** of the drug, with confinement in an institution, and carrying out the régime of drug administration, plus the administration of **strychnine**, which acted as an antidote, brought almost complete recovery and no recurrence of symptoms in 3 months.

Sir William H. Willcox (London Correspondent of J. A. M. A. 102:1168 (Apr. 7) 1934) in the *Lancet* repeats his warning that the barbiturates have a powerful action on the nervous system, and that care is required in their daily use. In therapeutic doses, symptoms such as mental depression, drowsiness, visual hallucinations, vertigo, ataxic gait, indistinct speech, squint, nystagmus, and paralysis of the limbs are common results. Prof. Richards, of Aberdeen, observed 3 cases in which loss of memory and automatism followed from daily therapeutic doses of the barbiturates and, as a result, an excessive number of tablets was unconsciously taken. In 1933, Willcox treated 8 cases of dangerous poisoning from barbiturates. Most of the deaths occur in persons who have been taking the drugs in repeated daily doses. He fully admits their value in the treatment of mental disorders.

From 1909 to 1914 there were admitted to the hospitals of Budapest 35 cases of barbital poisoning; while in 1932, one hospital of that city admitted 87 cases of barbital poisoning, in addition to 80 cases of poisoning from phenol barbital

*Prophylaxis and Treatment.*—Eric A. Freyworth (Brit. M. J. 1:304 (Feb. 17) 1934) makes an appeal to those of his colleagues who have to prescribe or dispense these dangerous drugs, never to prescribe them in tablets or in bulk, but to make it an invariable rule to prescribe them in divided powders and in combination with powdered ipecac and sugar of milk. This combination will have very salutary effects on anyone taking an excess quantity before the soporific can be absorbed in large amounts.

J. Purves-Stewart and W. H. Willcox (Lancet 1:6 (Jan 6) 1934) recommend the following procedure in cases of poisoning by barbituric acid compounds:

Every effort should be made to hasten the elimination of the poison from the body. Consequently, the **stomach** should immediately be **washed out** with warm water and this may be repeated at intervals of from 4 to 6 hours, 2 or 3 times. **Colonic lavage** should be given at once and repeated every 12 hours, 2 or 3 times. Since the coma is prolonged, **food** should be given **by a stomach tube** at intervals of 6 hours. This should include egg, coffee, dextrose, and peptonized milk in quantities of from 15 to 20 ounces (450 to 600 c.c.) From 15 to 20 ounces of **saline solution** and **dextrose** should be given by rectum every 12 hours.

Repeated hypodermic injections of **strychnine** in full doses are also valuable. **Lumbar or cisternal puncture and drainage** are carried out at intervals of from 12 to 24 hours, according to the symptoms of severity of the case. The application of cerebrospinal drainage removes the poison directly from the brain, on which the main toxic effect is manifested.

Cerebrospinal drainage appears to be the only form of treatment that gives a hope of recovery when pneumonia has commenced

**BISMUTH.** —*Therapeutics.*—WARTS —C. J. Lunsford, R. R. Thomson and G. W. Binkley (California and West Med 39:385 (Dec) 1933) treated with bismuth injections, 47 patients (39 adults and 8 children), for **warts**. Thirty-seven of the adults were given intramuscular injections of 1 c.c. (16 mms.) of *bismuth salicylate* in the gluteal region at weekly intervals. Of the 39 adults who cooperated, 11 were cured. Adults who were clinically cured received from 1 to 16 injections of bismuth salicylate with an average of 5.5 injections each, 2 adult patients were cured after 1 injection. An average of 7.5 injections was given to those cases in which treatment failed, 14 being the greatest number of injections.

In 8 cases in children, 50 per cent. were cured. This, with the 28.2 per cent of cures in the 39 cases of adults, would indicate that bismuth therapy has a limited place in the treatment of **verrucae vulgaris**. It would be justifiable to try it in cases of **multiple warts** on either **hands or feet**. Other cases where such treatment might be utilized would be washerwomen, surgeons, nurses, or children, where destructive measures are for any reason contraindicated.

The use of an aqueous 15 per cent. solution of *bismuth sodium tartrate* directly injected into the base of a wart is advocated by H. Shellow (Illinois M. J. 66:332 (Oct.) 1934). The skin about the lesion is prepared by washing with soap and water; iodine and alcohol are then applied. A fine hypodermic needle is used to pierce the skin just outside the zone of hyperkeratosis and directed downward and inward toward the base of the verruca at the most active point, the end of the needle remaining just above the corium. From  $\frac{1}{2}$  to 2 minims (0.03 to 0.12 c.c.) of the bismuth sodium tartrate solution is injected, according to the size of the lesion. In from 1 to 3 days after the injection a dark hemorrhagic area appears, visible through the keratotic surface. This denotes that the drug has taken effect. In the markedly keratotic hard type or ordinary verrucæ vulgaris, this phenomenon may not always be seen. In most cases, from 1 to 3 days after the first injection there has been either a complete cessation or a marked diminution of pain. The peripheral redness that so often accompanies the painful verruca disappears in from 2 to 7 days. All papillomatous lesions flatten out decidedly after the first injection, and in the plantar or palmar types the surface becomes smoother. If within 7 to 14 days following the appearance of the hemorrhagic center, the top of the verruca has not come off or the central portion has not fallen out, the keratotic tissue may be removed to determine whether or not any activity is still present. In most instances, after a lapse of from 14 to 17 days following the initial injection the removal of this hemorrhagic keratotic center reveals an underlying normal-appearing epidermis. If after 2 weeks of further observation, active verrucous tissue is seen, the lesion may be reinjected. Of 97 lesions, most of them having been previously treated by other measures, 89 were cured, 5 were improved, while 3 showed no improvement. Sixty-seven lesions were of the painful palmar or plantar variety, and 18 were of the verrucæ vulgaris type occurring on the dorsum of the hands and feet.

SYPHILIS—O. W. Bethea (Internat. M. Digest 24:309 (May) 1934) remarks that bismuth given by mouth is not absorbed sufficiently to be of therapeutic value in the treatment of syphilis. Nevertheless, S. Serefis (Med Klin 30:968 (July 20) 1934) has shown that bismuth subnitrate is changed into bismuth chloride not only by hydrochloric acid, but also by the chlorides of mineral salts. For the resorption of bismuth chloride it is important that it have a tendency to form complex compounds, such as with organic acids and their salts, or with polyvalent alcohols and with various types of sugar. Since the resorption requirements of bismuth orally administered are now known, therefore, there remains only the problem of the correct dosage to permit oral bismuth therapy of syphilis.

*Complications*—In general, it may be said that water-soluble salts are the most rapidly assimilated, produce the quickest response, and are the most likely to cause toxic symptoms, according to Bethea (*Ibid*). The principal toxic symptoms of bismuth when used for syphilis may be summarized as follows:

*Systemic*.—Headache, fever, malaise, and body pain, especially in the muscles and joints.

*Cutaneous.*—Symptoms closely resembling those of arsphenamine reactions. There may be pruritus, erythema (especially of a scarlatiniform type), urticaria, dermatitis, or even hemorrhagic lesions.

*Oral.*—There may be a blue line on the gums. This discoloration may often involve the tongue and other mucous membranes. There may be salivation, gingivitis and stomatitis. The stomatitis is milder than that produced by mercury and is not characterized by the marked discomfort and fetid breath of the latter. Most of these severe reactions have been reported from Europe, where comparatively large doses are usually employed.

*Gastrointestinal.*—Anorexia, nausea, vomiting, abdominal pain, and diarrhea.

*Local.*—There is usually some discomfort at the site of injections, but this is seldom of marked importance except where there has been faulty technic.

Most of the toxic manifestations require no further treatment than that of temporarily discontinuing the drug.

**NEUROSYPHILIS.**—In connection with the much discussed efficacy of bismuth in the treatment of neurosyphilis, Bethea (*Ibid.*) states he has been using, with excellent results, the following routine for the treatment of the milder types of neurosyphilis: For a period of 8 weeks there is a weekly removal of spinal fluid with the simultaneous intravenous injection of 0.6 Gm. (10 grains) of *neoarsphenamine* and intramuscular injection of 0.2 Gm. (3 grains) of *sodium bismuth thioglycollate*. Following this period the patient is given 6 weeks of *mercury* and *iodides*. This routine is repeated as indicated, due consideration being given to the necessity for prolonged treatment.

One of the greatest advantages of bismuth therapy is that it has enabled the clinician to maintain continuous treatment, and this great advantage is said to be the least understood by the profession as a whole. Bethea strongly advocates the continuous treatment which has been recommended by most syphilographers.

**BISMUTH SUBNITRATE.**—*Physiological Action.*—The use of bismuth subnitrate in hypertension, as advocated by E. J. Stieglitz (*J. Pharmacol. and Exper. Therap.* 46: 343 (Nov.) 1932) is not substantiated by C. Bruen (*Am. J. M. Sc.* 188: 21 (July) 1934). In 20 persons ranging from 27 to 73 with a median of 51 years, the administration of bismuth subnitrate was without demonstrable effect on the blood-pressure. The symptoms of dyspnea, palpitation, cardiac pain, dizziness and headache also pursued an independent course without reference to the administration or withdrawal of bismuth subnitrate. He concludes, therefore, that bismuth subnitrate by mouth, even in the largest therapeutically practicable dosage, does not develop sufficient nitrite action to exert any demonstrable effect on the blood-pressure or symptoms of arterial hypertension.

**BROMIDES.**—*Poisoning.*—Therapeutic doses of bromides may produce mental symptoms in susceptible individuals ranging from a mild clouding of the consciousness to an active delirium, and from an emotional and intellectual depression to stupor and coma. Possibly, due to the widespread use of the bromide, from 3 to 5 per cent of admissions to State hospitals have been found to be due to bromide intoxication, according to G. T. Harding, Jr., and G. T.



Harding, III (Ohio State M. J. 30:310 (May) 1934). The milder cases of bromide intoxication, resulting from the continued use of the drug, present coated tongue, bromide breath, dull headache, constipation, disinclination for either physical or mental exertion and psychic depression. Acne is the sign usually relied on as a warning. However, only in 3 of 18 cases did this symptom appear. The acute confusional states, overlooked until recently, present a variety of clinical forms. They resemble other acute organic or toxic reactions, such as those caused by encephalitis, uremia, alcohol, and other drugs. The intoxication proper may be divided into 3 clinical varieties, depending on bromide concentration in blood.

J. C. Sharpe (J. A. M. A. 102:1462 (May 5) 1934) reports 10 cases of intoxication from bromine in a general medical service. The symptoms of intoxication appear when from 25 to 30 per cent. of the chloride ion is replaced by the bromide. Only 1 patient developed a skin eruption. The discovery of a positive blood bromide reaction in a case of acute delirium or deep stupor modifies considerably what might otherwise be a grave prognosis. The diagnosis is simple. In all suspected cases, a *test* of bromide excretion in the urine is made rapidly and simply and is of sufficient reliability to rule out bromide intoxication. To 25 c.c. of urine add 1.0 Gm. of animal charcoal, mix well, allow to stand for a few minutes and filter. To 5 c.c. of the filtrate add 1 c.c. of a 30 per cent. gold chloride solution. A brown shade denotes a positive reaction.

**TREATMENT OF POISONING.**—In the treatment of bromide intoxication M. Levin (Ann Int Med. 7 709 (Dec.) 1933) recommends that the patient should be kept in **bed** until the intoxication has subsided. **Fluids** should be **forced**. If there is no nephritis, 4 Gm (60 grains) of sodium chloride should be given 3 times a day, the chloride ion facilitating the excretion of bromide ion. Patients who are *restless* should be given **continuous baths**. The need of using only the least toxic hypnotics is especially urgent in bromide intoxication, poisoned as the patients already are. **Paraldehyde** will suffice for the majority of cases. **Cardiac stimulants** should be given when indicated. Levin urges the following suggestions for the *prevention* of bromide psychosis:

- 1 When contemplating the administration of bromide, the physician should seek to ascertain whether the patient is already getting bromides from another source
- 2 He should know whether the patient takes much or little table salt. In the latter case, he should be doubly cautious
- 3 He should not relax his vigilance because the dosage he is giving is one that has proved harmless in the majority of patients
- 4 When a nervous patient getting bromides grows worse, the physician should promptly discontinue the drug unless he has good reason to believe that it bears no responsibility for the aggravation
5. When a patient has been taking bromides for a month or more, it is wise to occasionally discontinue them for a week or two

On the other hand, H. A. Paskind (J. A. M. A. 103 100 (July 14) 1934) considers that the impeachment of the use of bromides is unjustifiable. He believes that many physicians have come to use them timidly, ineffectually, or not at all, because of such authoritative statements, bolstered up by experience with the abuse of bromides.

A study of 54 patients with epilepsy, each of whom had taken bromide in sufficient amount to affect the seizure, for from 1 to 17 years, shows that only 3, or 5.5 per cent., became deteriorated. The occurrence of deterioration in this more adequately treated group was less than in a larger, less adequately treated series.

The misleading statements in the literature regarding the adverse effects of bromide in epilepsy are due to:

- 1 Failure to distinguish between intoxication and deterioration
- 2 The use of bromides in persons with epilepsy who were destined to deteriorate without their use.
3. The chance occurrence of behavior disturbances in insane or neurotic epileptic patients who had received bromide and in whom such behavior disorders occur without bromides

**CAFFEINE.—Physiological Action.**—The question of the deleterious effects of caffeine and coffee were studied by K. Horst, R. E. Buxton and W. D. Robinson (*J Pharmacol. and Exper Therap* 52:307 (Nov) 1934) They gave 14 men, from 20 to 25 years of age, caffeine or coffee (dosage, 3 or 4 mg ( $\frac{1}{20}$  or  $\frac{1}{16}$  grain) of caffeine per kg— $2\frac{1}{2}$  lbs—of body weight) once or twice a week and decaffeinated coffee on the intervening days. In certain studies, bouillon was administered as a control beverage. The blood-pressure and the pulse rate after decaffeinated coffee were essentially the same as after bouillon. After coffee or caffeine, the blood-pressure and the pulse rate were altered, although the changes were small and often uncertain. One or two hours after the drugs, the blood-pressure was usually increased (from 5 to 10 mm of mercury), the pulse rate decreased (5 per minute) in certain subjects and increased in others. Twenty-five hours after the drugs, the blood-pressure was not changed, but the pulse rate was at times increased. Motor function was changed by coffee or caffeine, the response to single doses being relatively uniform throughout the 2 months of experimentation. The performance of a simple movement (target test) was usually improved 1 or 2 hours after coffee or 5 hours after drugs. Caffeine exerted a sustained, deleterious influence on the performance of an acquired motor skill. Decaffeinated coffee did not affect performance of this skill. In the target test the effect of caffeine or coffee on performance was not apparent later than 25 hours after the drugs, but in the acquired motor skill each dose exerted an influence for several days.

**CALCIUM.—CALCIUM CARBONATE.—Therapeutics.**—In investigating how maggots effect a cure in *osteomyelitis*, M. A. Stewart (*Surg Gynec Obst* 58:155 (Feb) 1934) observed that during one stage, the maggots (*Lucilia sericata* Meig) exude calcium carbonate through their body walls. This is a very important finding, since it has been pointed out before (Beckhold, 1929) that calcium carbonate stimulates phagocytosis. It has also been known for some time that the bacteria excrete a leukocidin, which, unless removed or rendered inert, kills off the leukocytes as rapidly as they are attracted to the focus of infection. It has been previously supposed that the maggots cared for this exotoxin given off by the bacteria by absorbing it and rendering it nontoxic in their bodies through digestive processes. In order, then, to produce a chemical

substitute for living maggots, 2 steps were necessary, *viz.*: (1) suitable introduction into the wound of a form of calcium carbonate, in order to stimulate phagocytosis; and (2) a chemical means of removal from the focus of the accumulated leukocidin, a substance recognized as hampering phagocytosis. After prolonged experimentation on animals it was found that the leukocidin can be successfully rendered inert by exposure to a dilute aqueous solution of *picric acid*, while the *calcium carbonate* may be introduced in the form of an aqueous suspension.

Briefly, the treatment consists of the following steps: (1) After an operation, when the necrotic bone is removed surgically, the wound is packed for 24 hours with vaseline gauze, in order to allow the trauma to subside. (2) At the end of this period the gauze packing is removed and the wound is thoroughly irrigated with the picric acid solution (0.25 per cent. aqueous solution of picric acid to which 8 per cent. glycerin has been added) by means of a syringe. (3) Within a few seconds' time an aqueous suspension of calcium carbonate (20 Gm.—5 drams—of calcium carbonate to 215 c.c.—7½ ounces—of distilled water) is sprayed into the wound by means of a nasal atomizer, until a thin layer of a white precipitate of calcium picrate is laid down over the osseous and soft tissues. These treatments may be carried out about 3 times a week, unless the condition is very acute, when daily dressings are recommended.

**CALCIUM CHLORIDE.**—*Dose.*—T. Z. Gurevich (Sovet. vrach. gaz. 17 1252 (Sept 15) 1934) used calcium chloride in large doses in the treatment of 15 patients upon whom the usual diuretics were not effective. Daily doses of from 10 to 30 Gm (½ to 1 ounce) did not give rise to any serious untoward symptoms. In 4 patients there developed nausea and anorexia, but these symptoms disappeared on the withdrawal of the drug and were not present when its ingestion was resumed a few days later. The diuretic effects became manifest only after a number of days, occasionally weeks. Large doses may produce an exacerbation of a nephritic process while acting as a diuretic. The calcium chloride is effective when salt is eliminated from the diet.

*Therapeutics.*—In the treatment of **pleural effusion** occurring in the course of **artificial pneumothorax**, J. Foix and E. Grunwald (Presse méd. 42 3 (Jan. 3) 1934) use a 6.6 per cent. aqueous solution of calcium chloride, of which solution the patient ingests from 6 to 12 spoonfuls a day. They have seldom observed symptoms of intolerance (vomiting, diarrhea) and attribute this to the low concentration of their solution. Often, they have administered calcium intravenously in addition to that taken orally, and injected twice weekly 10 c.c. (2½ drams) of a 1:10 solution of calcium gluconate. In 24 of 48 patients thus treated, they obtained a rapid defervescence of the temperature, in 13, the defervescence was obtained in from 6 to 7 hours, and in 11, the defervescence lasted for 10 days. Among 24 patients in whom the results of this therapy were disappointing, 3 had purulent pleurisy, and 12, old pleural effusion. Calcic therapy has its best chance for success when it is begun immediately after the appearance of pleural inflammation.

In some cases the calcic therapy was without effect, although it was started at the beginning of the purely inflammatory stage of pleural effusion. According

to Blum's theory, natural or artificial inflammation of the pleura may occur only in the presence of sodium. The exudates are essentially composed of water, protein and sodium chloride. On ingestion of calcium chloride, the calcium displaces the sodium and by eliminating the sodium and water, stops the inflammation. Since this therapy appeared efficacious in 70 cases out of 100, generally speaking, it is believed desirable to use this inoffensive calcic therapy systematically, so as to combat the menace of pleural effusions that occur during the course of artificial pneumothorax.

**CALCIUM GLUCONATE.**—During the last trimester of *pregnancy*, one of the most frequent complaints noted by C. E. White (J. Oklahoma M. A. 26:388 (Nov.) 1933) has been tingling and numbness of the hands and feet together with cramps of the legs. These complaints are frequently associated with pains in the hips, stiffness, and inability to walk comfortably after rising. He was not impressed by the opinion that such complaints are due to polyneuritis of pregnancy. For some time White has been using calcium gluconate and dicalcium phosphates for this type of patient and reports absolute relief of symptoms in 2 or 3 days without other therapy. They will tolerate this medication in large doses.

This view is concurred in by G. W. Theobald (Brit. M. J. 2:376 (Aug. 26) 1934), who states that if excessive salivation, vomiting, cramps, dermatitis herpetiformis, edema and other symptoms can be cured by the injection of calcium, it is logical to suppose that they are caused by its deficiency. The number of patients who have been treated is small, but the success that attended calcium therapy in such a variety of conditions warrants its extended trial. He claims that a complete, well-balanced, appetizing and easily digested diet, rich in the vitamins and in calcium, iron and iodine, if given early in pregnancy, will prevent the onset of toxemias, although it may be necessary to increase the available amount of calcium by the injection of calcium gluconate. Indeed, it might be expedient, and in the end economical, to give routine injections of this mineral at the thirty-second and thirty-sixth weeks of pregnancy.

The daily dose of 60 grams (4 Gm.) of calcium gluconate by mouth for 10 to 14 days before the onset of the menstrual period and continued through the first two days of the period was tried in 49 cases of essential *dysmenorrhea* by R. E. Boynton and E. C. Hartley (Am. J. Obst. and Gynec. 27:253 (Feb.) 1934). Thirty-three of the patients were greatly benefited, but 16 seemed to receive no help. An alkaline mixture, which was used alone in a few cases and with calcium gluconate in other cases, consisted of equal parts of magnesium carbonate and sodium bicarbonate in dosage of 60 grams (4 Gm.). This was used 3 times a day, for 10 days, before the onset of menstruation. Corsswell and Winter have shown that with adequate phosphorus intake, magnesium appears to favor calcium storage instead of calcium loss.

The faulty response to calcium therapy is usually due to inadequate dosage and faulty instruction as to the method of administration, according to A. Cantarow (Pennsylvania M. J. 37:457 (Mar.) 1934). Calcium gluconate must be given in doses of 60 grams (4 Gm.), and the lactate and chloride in doses of 20 to 40 grams (1.3 to 2.6 Gm.), 3 to 4 times daily. The dosage for children

must be calculated on the basis of the body weight. All calcium salts should be administered about 4 hours after or  $\frac{1}{2}$  hour before meals, preferably in water. No food should be taken between meals, with the possible exception of lactose.

Calcium therapy has been used to effect desensitization in rheumatic disorders by I. Zenoff (Wien. klin. Wchnschr. 47:235 (Feb. 23) 1934). He controlled the curative process by determining the sedimentation speed of the erythrocytes. He found that, particularly in the acute forms of rheumatism, the accelerated sedimentation was gradually normalized under the influence of the calcium therapy. Fifty-five patients with *acute articular rheumatism* were given daily injections of 10 c.c. ( $2\frac{1}{2}$  drams) of **calcium gluconate** (in all, from 15 to 25 injections). In addition to this, they were given **sodium salicylate** by mouth—on the first few days 12 Gm. (3 drams) and later less. This treatment counteracted the fever in from 10 to 26 days. Injections of calcium gluconate were used as the only therapeutic procedure in 23 cases of acute and 28 of *chronic rheumatism*. In these cases the first few injections of calcium gluconate frequently caused an acute exacerbation, but finally the calcium injections effected a complete remission. Aside from counteracting the pain and restoring the mobility of the joints, the treatment has the advantage that cardiac impairments rarely develop. When the treatment was conducted in the proper manner (control of sedimentation of erythrocytes), relapses were never observed within a year.

**CALCIUM ORTHO-iodoxybenzoate.**—*Therapeutics.*—This remedy has been used in the treatment of *arthritis* by T. Wheeldon (Ann. Int. Med. 7:1540 (June) 1934). It seemed suitable for the following reasons:

- 1 It is not related to cinchophen or other quinoline derivatives, which, when used without close supervision, may cause severe allergic manifestation or hepatic damage.
2. The patient does not become addicted to its use.
- 3 Only occasionally do patients complain of nausea or other gastrointestinal disturbances following its ingestion.
- 4 Apart from the objective improvements effected, it gives the patient a subjective sense of improvement which helps him to continue with his régime.

Patients who have been chronic invalids for months or years were restored to useful activity. It may be noted that where intense discomfort is present, calcium ortho-iodoxybenzoate may be given conjointly with salicylates or other analgesic drugs apparently without fear of incompatibility. X-ray studies showed no evidence of progression of the joint changes characteristic of atrophic or hypertrophic arthritis.

**CARBON DIOXIDE.** — *Administration.* — Carbon dioxide being a respiratory stimulant, it is important to maintain the supply in the administration of **gaseous anesthetics**, according to J. G. Poe (Surg. Gynec. Obst. 58:711 (Apr.) 1934). With open ether administration, he maintains, there is "practically no control of respiration" and the conservation of carbon dioxide is limited to the amount that may lodge in the mask to be reinhaled. This results in slow and shallow respiration, hyperpnea, with acapnia, apnea, and often excitement and struggling. At Baylor University Hospital a complete rebreathing method

is used for the induction of anesthesia; the apparatus employed consists of a face-piece, rebreathing bag, and a tank carrier. There are no measuring devices, but the process of administering the anesthetic is individualized, the anesthetist using each gas as he desires. With this method anesthesia is induced with nitrous oxide gas, oxygen changing to ethylene, with or without ether, as may be required. With the degree of humidity in the bag obtained by this method and the percentage of carbon dioxide accumulating, ethylene is a safe anesthetic without danger of ignition. Carbon dioxide may be added, when necessary, to maintain satisfactory respiration; and carbon dioxide with an over amount of oxygen is often given at the end of the operation to insure full oxygenation and inflation of the lungs. With this method narcotic premedication is used without danger of respiratory depression. Patients recover rapidly from the anesthesia and the incidence of pulmonary complications is very low. In 1032 appendectomies at the Hospital from June 1, 1930, to Feb. 1, 1933, there was only one pulmonary complication. For the first 6 months of 1933, in all operations at the Hospital, there were only 8 postoperative pulmonary complications, with 1 death, and in the following 4 months, there were no pulmonary complications.

**Physiological Action.**—The effect of carbon dioxide inhalation on the blood coagulability and bleeding time in man and animals was investigated by J. Marx (Arch. f. klin. Chir. 178:170 (Nov. 29) 1933). He found that if guinea-pigs were kept from 3 to 5 minutes in an air mixture containing 5 per cent. by volume of carbon dioxide, the blood coagulation time is diminished by 33.5 per cent. and the bleeding time by 29 per cent. In healthy people after from 4 to 5 minutes of continuous inhalation of this air mixture there was 45.3 per cent. diminution in the blood coagulation time and 68.2 per cent. diminution in the bleeding time. Five minutes later, these values showed a diminution of 53 and 70 per cent., respectively, and after  $\frac{1}{4}$  hour still showed 26.5 and 25 per cent., respectively. In comparison with this, the number of thrombocytes 15 minutes after inhalation showed a rise of 22.7 per cent. The blood coagulation time in a cholemic dog after 10 minutes of continued inhalation was reduced about 52.8 per cent.; after 5 minutes, it was reduced about 44.5 per cent., and after 15 minutes, reduced about 29 per cent. The bleeding time correspondingly showed a diminution of 29.6, 16, and 28 per cent., respectively. After repeated inhalations, the coagulation time sank to 39.5 per cent. and the bleeding time to 30.8 per cent. In patients suffering from icterus with retarded blood coagulability and bleeding time, a diminution of the former 44.7 per cent. may be observed after 15 minutes, while that of the latter may be found to be 39.8 per cent. On the basis of these experiments, it is recommended that from 4- to 5-minute inhalations be administered before the operation in already existing *parenchymatous hemorrhages* or as an effective prophylactic.

**Therapeutics.**—P. Faraga (Ztschr. f. d. ges. exper. Med. 91:114 (Oct. 21) 1933) shows that, in addition to the medicinal and dietary treatments, carbon dioxide inhalation has a certain place in the symptomatic treatment of *bronchial asthma*. He found that some asthmatic attacks and dyspneas may be favorably influenced by the inhalation of an 8 per cent. mixture of **carbon dioxide** and **oxygen**. The inhalation of this mixture effects a decrease in the alkali reserve

and an increase in the lactic acid content of the blood. The *pH* of the urine remains the same, while the ammonia elimination decreases.

The use of carbon dioxide in concentrations of 5 to 7 per cent. in *lobar* or *bronchopneumonia* appears to A. L. Barach (New York State J. Med. 34:672 (Aug. 1) 1934) unsupported by the theoretical and clinical evidence now available. This type should be employed in conditions in which depressed respiration is present, in which its value has been fully substantiated.

**CARBON MONOXIDE POISONING.**—Highway accidents and asphyxiations from carbon monoxide greatly exceed all other forms of violent death. Consequently, the investigation of such deaths constitutes a very large and important part of the medical examiner's work

In New York during a 5-year period (1928 to 1932) there were 5289 deaths from carbon monoxide poisoning. This is an average of over 1000 deaths a year. H. S. Martland (J. A. M. A. 103:643 (Sept. 1) 1934). As a cause of violent death it is exceeded only by highway accidents, which for the same period averaged 1400 a year. It is highly possible that in some of the automobile accidents with undetermined causes, the dulling of the reaction time, when quick coordinated movements are required, may be due to small amounts of carbon monoxide.

**Symptoms.**—As given by H. M. F. Behneman (Northwest Med. 33:301 (Sept.) 1934), these change with the degree of blood saturation. Thus, up to 10 per cent blood saturation produces no symptoms; 10 to 20 per cent., tightness across the forehead, possibly slight headache, dilatation of cutaneous blood-vessels; 20 to 30 per cent, headache and throbbing in the temples; 30 to 40 per cent, severe headache, weakness, dizziness, dimness of vision, nausea and vomiting, collapse, 40 to 50 per cent, same as above, with more collapse, syncope, increased pulse and respiration, 50 to 60 per cent, as above, coma with intermittent convulsion, depressed heart and respirations, Cheyne-Stokes breathing, 60 to 70 per cent, coma and as above, possibly death, 70 to 80 per cent, weak pulse and slowed respiration, respiratory failure and death

Generally, the symptoms resemble those of anoxemia produced in other ways, except that there is a greater tendency to faint in this intoxication. Thus, the exposed person may collapse before he realizes the danger to which he is exposed. The body temperature is lowered, but there is fever upon recovery from the intoxication. Individual susceptibility varies, and a moderate tolerance can be acquired.

**Diagnosis.**—In reference to the detection of carbon monoxide poisoning as a cause of death, Balthazard and Melissinos (Paris méd. 2. 393 (Nov. 18) 1933) state that the variation of the coefficient of toxication in carbon monoxide poisoning is due to physiologic causes and does not impair the theory which attributes death in carbon monoxide poisoning to anoxemia. They found that in all cases in which the value of the coefficient was between 0.42 and 0.8, carbon monoxide was, if not the sole, at least the principal cause of death. This is not the case if the coefficient has a value of less than 0.42, which is plausible only in cases in which the period of survival is more or less prolonged. Coefficients of 0.05 or less, regarded by some authors as a sign of carbon monoxide poisoning, denote,

on the contrary, that death is due to some other cause. The organism can withstand without inconvenience doses of carbon monoxide corresponding to coefficients of 0.1, 0.2 and even 0.3. Such values might be observed in persons remaining near a fireplace or a poorly installed heating plant without any experience of discomfort on their part. If these persons are found dead, their death must be attributed to some cause other than carbon monoxide poisoning. The finding of values below 0.42 in manifest cases of carbon monoxide poisoning may be due to technical errors in determination of coefficient or to putrefaction of the reduced hemoglobin (with preservation of that combined with carbon monoxide) in cases in which examination is made long after death. It was demonstrated experimentally that reduction of the oxygen content in the atmosphere lowers the coefficient of carbon monoxide intoxication and, inversely, increase of the oxygen content raises the coefficient. The administration of pure **oxygen**, preferably under pressure, is considered the only rational and efficacious therapy in carbon monoxide poisoning.

**Prophylaxis.**—The chief factors in the prevention of carbon monoxide poisoning, according to H. M. F. Behneman (*Ibid*), are (1) good ventilation; (2) avoidance of air known to contain the gas; (3) adequate protective equipment: gas appliances, proper use and fittings; use of gas masks when in bad air, respirators for self rescue and other rescue work; (4) education and diligence in keeping in mind the possibility of exposure from many sources to a gas that gives little or no warning of its presence, (5) proper inspection and examination of all working areas before placing men to work and during their work, (6) the use of canaries or chemical tests at stated intervals when work is being done in areas of possible dangers.

**Treatment.**—Carbon monoxide asphyxia has received so much publicity that an increasing number of investigators are offering new methods of treatment. The proposed remedies are mainly respiratory stimulants. The evidence offered for them is that animals asphyxiated to the point of failure of respiration survive if the drug is administered instantly. Clinically, the physician must apply the remedy at almost the exact instant at which respiration fails. If he arrives 10 or even 5 minutes later, the victim will be beyond recovery. Owing to the fact that the respiratory stimulant drugs (such as lobeline or methylthionine chloride) have deleterious effects on the heart and circulation, the patient may be better next day if the drug is not administered. Asphyxia and respiratory failure are by no means the same, even if the one may lead to the other. A patient comatose from asphyxia, and likely to die some hours later, is often breathing with even more than normal vigor. What he needs, and all that he needs, is removal of the carbon monoxide, restoration of the oxygen-transporting power of the blood and replacement of the carbon dioxide that has been lost during the development of asphyxia. None of these steps toward recovery, according to Henderson and Haggard, can be promoted to any considerable degree by any hypodermic medication, but they are all directly achieved by the **inhalation of oxygen** and from 7 to 10 per cent of **carbon dioxide**. This treatment is now well-established, theoretically, and has saved so many hundreds of lives that it must still be considered the method of choice. Since the introduction of the inhalational treat-



ment of carbon monoxide asphyxia, the deaths from illuminating gas poisoning in New York City for the 6 years ended with 1932 have been as follows: 611, 570, 525, 305, and 278. This is a striking demonstration of the effectiveness of this treatment.

*Active Therapy.*—Recovery depends largely upon the elimination of carbon monoxide from the blood, and this, in turn, depends upon the percentage of oxygen in the air breathed and the rate and depth of respiration.

The most effective plan of treatment, advocated by Behneman (*Ibid*), is as follows:

1. Either **carbon dioxide** (5 per cent.) and **oxygen** (95 per cent.) **inhalation** or,
- 2 **Oxygen** (pure) **inhalation**; from 20 minutes in mild cases to 3 hours in severe cases. Continue it until the carbon monoxide is eliminated from the blood.
3. **Fresh air** until or when the above two gases are not available. This may mean **artificial respiration**, preferably by the commonly used Schäfer method. Get the victim into fresh air as soon as possible.
4. **Absolute rest** lying down.
- 5 **Fluids**, by rectum if necessary.
6. Build up resistance; **ample diet, force fluids, catharsis.**
7. Stimulants as needed, using **strophanthin, digitalis, strychnine** or **atropine with caution** Use **massage, hot blankets and hot bags.**

It is well to keep in mind this fact: When the victim of carbon monoxide poisoning is first discovered, it should be remembered that conditions which rendered that person unconscious may still be existing, so that for the safety of the attendant as well as that of the victim, **immediate exit to fresh air** is indicated and important. No matter how near death the victim may seem, immediate and persistent treatment often accomplishes amazing results.

**CARBON TETRACHLORIDE.**—This drug has many uses at the present time. Many years ago it was tried as an anesthetic in place of chloroform, but was found to be too toxic because of the high chlorine content. More recently, it has been given as a remedy in hookworm and other intestinal parasitic diseases. It is at present being used by the veterinary profession in treatment of canines. Perhaps the most frequent commercial uses of carbon tetrachloride today are the following

- 1 As a solvent in the rubber industry
- 2 As a cleansing agent in the dry cleaning industry
- 3 As a solvent in the chemical and drug industry
- 4 As an occluding and nonoxidizing agent in fire extinguishers
- 5 As a solvent in the paint industry.
- 6 As an anthelmintic for parasites in the practice of medicine.
7. In machine shops for the removal of grease in combination with benzine, in order to keep the fire hazard at a minimum.
8. As a dry shampoo in the hair dressing industry, especially in foreign countries.

The chief use of carbon tetrachloride in all of these processes is as a solvent and diluting agent to reduce the flash point in certain other solvents

**Poisoning.**—From experiment and examination of many persons exposed to carbon tetrachloride fumes, P. A. Davis (J. A. M. A. 103:962 (Sept. 29) 1934) states that the following *symptoms* may be caused: slight headache; nausea (in many cases this becomes severe and lasts for several days); nervousness; mental confusion; loss of weight; dry dermatitis; secondary anemia; slight jaundice; chronic spasms of muscles; necrosis of the liver; acidosis; phosphaturia; loss of consciousness, coma and death; visual disturbances, such as blurred vision, color confusion and disturbance of near vision. He recommends the following *treatment* in these cases:

(1) **Removal from contact** with the substance; (2) **aeration**—fresh air, oxygenated, if necessary; (3) **alkalinization** with **sodium carbonate**, **calcium carbonate** or intravenous **calcium gluconate**; (3) ingestion of **levulose**, **dextrose** and **animal fats**; (4) **tincture of digitalis** to protect the heart; (5) **hexylresorcinol** for kidney irritation; (6) intravenous administration of **physiologic solution of sodium chloride** and **dextrose** or **Fischer's solution**; (7) **transfusion** if necessary, followed by the administration of **iron compounds**; (8) if any *bronchial conditions* develop, which is common after the use of certain impure grades of carbon tetrachloride, owing to the free chlorine and carbonyl chloride, inhalations of **compound tincture of benzoin** and **pine needle oil**, followed by some **soothing syrup containing codeine**, unless the condition of the kidneys and liver contraindicate it; (9) **free catharsis**; (10) **forced liquids and starchy foods**.

Epinephrine should not be used in cases of carbon tetrachloride poisoning if there is a possibility of any myocardial involvement.

In the therapeutic use J. W. Tomb and M. M. Helmy (J. Trop. Med. 36:334 (Nov. 1) 1933) found that carbon tetrachloride is capable in therapeutic doses of causing fatal intoxication accompanied by acute degeneration of the liver. Fatalities occur much more frequently among children. This is probably due to an insufficiency of calcium reserves in the young. Immediate poisoning in therapeutic doses is generally associated with disease of the liver or with other clinical contraindications. Delayed poisoning is generally due to nonelimination of the drug from the intestinal tract. It may be obviated when the liver is healthy by rapid and free evacuation of the drug. In Egypt, fatal intoxication by carbon tetrachloride has been found to be closely associated with ascariasis. When intoxication has manifested itself, intensive treatment by intravenous injections of **calcium gluconate** (Sandoz) is capable of saving life, provided the drug has been thoroughly evacuated from the intestinal canal.

**CHOLINE.**—Choline and its ester, acetyl choline, have been known for several years and a considerable bibliography has accumulated regarding their effectiveness in a variety of pathologic conditions due to vascular spasm, particularly of the peripheral vessels. The usefulness of **acetyl choline** has been limited by the fact that being rapidly destroyed by body fluids, it is without effect when given by mouth, and its action is very slight when administered subcutaneously. Intravenous administration is regarded as dangerous and at best gives only transient effects.

Investigation has shown **acetyl-beta-methylcholine chloride** to have the following advantages over acetyl choline: (1) Its hydrolysis in blood is very much slower; (2) it is much more potent when injected subcutaneously; (3) it produces effects when taken by mouth; (4) it lacks certain of the undesirable side-effects of acetyl choline, *i. e.*, its nicotine-like effects. It is a physiological antagonist to epinephrine. Its action is entirely prevented or abolished by atropine.

**Therapeutics.**—In 29 attacks observed in 9 patients by I. Starr, Jr., K. A. Elsom, J. A. Reisinger, and A. N. Richards (Am. J. M. Sc. 186:313 (Sept.) 1933) and J. H. Comroe, Jr. and I. Starr, Jr. (J. Pharmacol. and Exper. Therap. 49:283 (Nov.) 1933) with *paroxysmal tachycardia*, the attacks usually stopped within 2 minutes after the drug's action commenced. The dose of acetyl-beta-methylcholine used was 30 mg. ( $\frac{1}{2}$  grain) given subcutaneously (never intravenously). If the attack does not stop within a minute, the spot of injection should be massaged.

J. Kovacs (Am. J. M. Sc 188.32 (July) 1934) used a 1 per cent. solution of acetyl-beta-methylcholine chloride (1 Gm.—15 grains—in 100 c.c.— $3\frac{1}{3}$  ounces—of water) in treating 40 cases of *chronic rheumatism*, 16 of rheumatoid arthritis, 14 of osteoarthritis, 3 of bursitis, 3 of sciatica, and 4 of neuritis. Reinforced asbestos fabric paper is saturated with the solution and wrapped around the affected joints.

The most promising results were obtained in the most stubborn cases of *rheumatoid arthritis*; 95 per cent. of the cases showed improvement. In the *osteoarthritic type* the results were likewise encouraging, giving definite improvement in 80 per cent. of the cases. There was full recovery in the 3 cases of *sciatica*, in which previously diathermy and galvanic treatment had failed to give relief. In the 3 cases of *bursitis*, 2 responded quickly but in the third case the treatment failed to give relief. The 4 cases of *neuritis* reacted well to the treatment and in every case there was full and speedy recovery. In the few cases of *peripheral vascular disease* treated, desirable results have been obtained; release of spasm with increased circulation.

In brief, the method consists in thoroughly wetting a strip of reinforced asbestos paper with a 0.25 to 0.5 per cent. aqueous solution of acetyl-beta-methylcholine. The sheet is wrapped around the affected limb but not directly over an open ulcer. Over the sheet is placed the positive electrode of galvanic machine (not diathermy). The negative electrode is placed on some other part of the body, usually the back. Both electrodes should be very firmly and evenly applied. About 45 volts and 20 to 30 ma. of current are applied for 20 minutes to  $\frac{1}{2}$  hour. Occasionally a patient indicates some difficulty in breathing. If this occurs, it is advisable to discontinue the treatment. To prevent shocking the patient, it is necessary to turn the current on and off very slowly. It is necessary also to avoid having the metallic electrode touch the flesh at any point, as this will cause a burn.

Following the treatment it will be noticed that the skin has a "gooseflesh" appearance which quickly disappears and is followed by a distinct hyperemia and

profuse sweating, with local elevation of temperature of 4 to 10° F., which persists for 3 to 4 hours.

During the course of treatment the patient has a pleasing sensation of warmth throughout the body, but particularly in the limb being treated. There is usually a moderate fall in blood-pressure and an increase in salivation, particularly if the application is made on the upper limbs. In some instances there is also evidence of an increased peristalsis and an urgent desire to urinate. Subjectively, the patients obtain considerable relief from painful symptoms, and objectively, it will be noticed that there is considerable improvement in mobility in the affected joint, together with lessening of the swelling.

**CINCHOPHEN.**—*Toxicity.*—An additional number of cases of toxic cirrhosis from cinchophen have been reported. S. D. Conklin (Pennsylvania M. J. 37:827 (July) 1934) reports 5 cases in the past 18 months. C. L. Short and W. Bauer (Ann. Int. Med. 6:1449 (May) 1933) report 4 cases in whom urticaria developed following administration. One case showed an abnormal van den Bergh, and damaged liver function by the Rosenthal test. Prompt cessation of the drug did not prevent the development of the clinical symptoms of acute yellow atrophy 2 weeks later. Forty-one cases are reviewed. The amount of the drug used before the symptoms appeared varies from 1 to 115 Gm ( $\frac{1}{4}$  to  $3\frac{3}{4}$  drams). The duration of administration was 2 weeks or less, in all but 5 instances. Although urticaria was the most common type of allergic manifestation to occur, it sometimes took the form of a scarlatiniform, purpuric, morbilliform, vesicular, or bullous eruption, aphthous ulcers in the mouth, or syncope with vasomotor collapse. In 6 cases the allergic manifestations must be considered an indication for the **immediate** and **final withdrawal** of cinchophen in all its forms, and *prophylactic* administration of **glucose** for at least 1 week.

M. W. Comfort (Minnesota Med. 17:237 (May) 1934) states that, undoubtedly, some individuals have an unexplained idiosyncrasy to the drug and until some method to detoxify it is found, certain precautions should be taken when cinchophen is used. When medicine has been taken to alleviate pain prior to the onset of jaundice, the suspicion should be entertained that the medicine was cinchophen.

The *treatment* of cinchophen intoxication is based upon a liberal intake of **carbohydrates**, with encouragement of the patient toward a plentiful supply of such foods. Candy, Karo syrup and bread should be within easy reach of the patient. **Glucose**, 10 per cent, and **sodium lactate**, 2 per cent, intravenously, in daily quantities from 1000 to 3000 cc (1 to 3 quarts), have been of much value, **duodenal drainage**, if the patient's condition permits; **insulin** may increase the efficiency of the glucose, **liver extract** and **diathermy** have their advocates.

In the nonfatal cases, the jaundice usually begins to clear within 3 weeks, and recovery is fairly complete in 8 weeks.

**COD-LIVER OIL.**—*Therapeutics.*—In a bacteriologic study of various fats and oils, W. Lohr (Zentralbl. f. Chir. 61:1686 (July 21) 1934) found that they are usually bacteria-free even when not sterilized. Bacteria ordinarily

encountered in infected wounds, streptococci, staphylococci and *Bacillus coli*, perish when introduced into cod-liver oil. It has not been determined whether they die because the cod-liver oil contains no nourishment for them or because of the surface tension of the oil. It was further demonstrated that large amounts of the cod-liver oil used in the treatment of extensive **wounds** did not cause toxic manifestation of any kind. The oil was used in combination with indifferent substances to give it the consistency of a paste. In this salve the oil permeates the tissues and causes a rapid liquefaction of the necrotic tissues, followed by a powerful stimulation of the growth, which affects all tissues, including the epithelium. Large areas fill with granulation tissues and these become covered with regenerated epithelium. The inhibiting effect on the bacterial flora of wounds was likewise striking. The technic of treatment of fresh industrial wounds consists of the usual toilet of the wound with omission of suturing. A thick layer of the cod-liver oil is laid on the wound surfaces and in the case of an extremity, a plaster-of-Paris cast is applied over it. The cast is removed at the end of 14 days, when the lesion is usually found to be healed. This treatment is not applicable to wounds badly soiled with earth or highly infected by paranaemia, or to gas bacillus infections. The cod-liver oil treatment is resorted to only after the infection has been overcome, in order to obtain good regeneration. On the other hand, the treatment finds its application in chronic wounds, even if infected.

A method of treating **acute osteomyelitis** by the use of cod-liver oil is explained by W. Lohr (*Arch. f. klin. Chir.* 180:206 (Sept. 21) 1934). He reports 24 cases of acute osteomyelitis of the long bones treated with cod-liver oil and a plaster cast. The field of operation was rendered bloodless and a long incision was made over the tender part of the bone. The periosteum was split and pus evacuated. He seldom found it necessary to drill the bone. The wound was filled with cod-liver oil, and the skin incision was loosely closed with interrupted sutures. A circular plaster cast was applied. In the next few days a profuse discharge of an emulsion of pus and oil took place. The behavior of the wound could be judged from the temperature curve, the appearance of the tongue, the appetite and the sleep. The cast was removed at the end of the second or the third week, at which time x-ray examination gave an accurate idea of the extent of the involvement. The patient at this stage was submitted to a second operation, in the course of which sequestrums were removed and the bone cavity was filled with cod-liver oil. Later it was shown that the second operation could be dispensed with in a high percentage of the cases. Of the 24 cases, 6 belonged to the most severe type not amenable to any local treatment and ended fatally. Of the remaining 18, the temperature fell promptly in 17 patients. In one the temperature remained elevated and a more radical operation was repeated at the end of 2 weeks. All 18 patients were discharged as cured. The convalescence was smooth and painless. It is believed that, with this method a high percentage of cases of acute osteomyelitis may be definitely cured and thus prevented from passing into the stage of chronic osteomyelitis. The principle of the treatment is not to disturb the tissues. The use of disinfectants, drains, gauzes, and frequent dressings is entirely omitted. Of 26 patients with chronic

osteomyelitis given the treatment, 1 died of embolism, 3 were not cured, and 21 were completely cured and discharged without fistulas.

Cod-liver oil in the treatment of **burns** was found remarkably effective by W. Lohr (Chirurg. 6: 263 (Apr.) 1934). It controls the secondary infection of large areas. A rapid cleansing of the wound follows its application, and epithelization is stimulated to a degree not seen in any other form of treatment. It is superior to the tannic acid method in that it may be used on the face and in such difficult regions as the buttocks, scrotum and anus. The cod-liver oil was used as salve or in combination with the cod-liver oil plaster-of-Paris cast. Attention is called to the fact that commercial cod-liver oil is sterile. Under the influence of the oil and the rest secured by the cast, extensive and deep ulceration in most difficult locations heal in the surprisingly short period of from 8 to 14 days. The closed method of treatment with the cod-liver oil plaster-of-Paris cast is particularly applicable in second degree burns of the extremities. Secretions may be copious in the first few days and make it advisable to replace the original cast. As a rule, the cast is kept on for 2 weeks. Third degree burns of the extremities are treated by enfolding the extremity in sterile towels thickly covered with the cod-liver oil salve.

From a clinical study and analysis of 948 cases of patients who received various **antirachitic** agents over a 5-year period, A. De Saicetes and J. D. Craig (New York State J. Med. 34: 712 (Aug. 15) 1934) arrive at the following conclusions, which are very valuable at this time in view of the claims being made for the newer preparations and the relative expense involved:

- 1 Cod-liver oil in liquid form—3 teaspoonfuls daily (8932 to 13,000 U. S. P. X. units of vitamin A and 3,057 A. D. M. A. vitamin D units)—gives almost complete protection against rickets

- 2 Cod-liver oil concentrate in tablet form—3 tablets a day (6300 U. S. P. X. units of vitamin A and 1500 A. D. M. A. vitamin D units)—gives almost the same degree of protection

- 3 Viosterol in 100 X, 250 X and 500 X (7300 to 36,000 vitamin D units, no A units) gives only slight protection

- 4 Carotene (3500 A. units, no D units) does not give protection

- 5 The addition of carotene to 500 X viosterol (36,000 D units and 1750 A units) gives almost 90 per cent. protection. It is significant that the addition of pro-vitamin A decidedly increases the degree of protection

- 6 We are yet of the opinion that rickets are not due to a deficiency of vitamin D alone, but that Vitamin A is an important factor in this disease. Because of the fact that even 10 times as many D units in the form of viosterol do not give the same protection as cod-liver oil, it is fair to assume that the D factors in viosterol and cod-liver oil are not identical

**CYANIDE POISONING.—Treatment.**—Successful chemical antidotes in the treatment of experimental cyanide poisoning are **methylene blue**, **sodium nitrite**, **triase** and **sodium thiosulphate**. Within limitations, all these agents, except triase, which has not been tried in man, have a demonstrated clinical usefulness. Their actions are both protective and resuscitative.

P. J. Hanzlik and A. P. Richardson (J. A. M. A. 102: 1740 (May 26) 1934), as a result of vast animal experimentation, conclude

1. Experimentally effective in protective and resuscitative treatments of fatal cyanide poisoning, and clinically useful, in order of decreasing efficiency, are a combination of sodium

nitrite and sodium thiosulphate, sodium nitrite, methylene blue and sodium thiosulphate. Experimentally effective, but clinically inadvisable, is triose (glycerinic aldehyde).

2. In mammals, probably including man, the antidotal actions in cyanide poisoning of the following are mediated predominantly through methemoglobin formation: Nitrite-thiosulphate combination, nitrite, methylene blue and toluidine blue. Triose apparently forms cyanhydrine and is assisted by central stimulant actions. Thiosulphate is a direct oxidant of cyanide with formation of sulphocyanate.

3. Some kind of direct action, in part at least, on mammalian tissues and cells, independently of methemoglobin, is postulated for methylene blue, and such action is predominant in antagonizing cyanide poisoning of simple physical and biologic systems.

4. The most interesting of a number of ineffective agents are ethylene blue, which is chemically close to methylene blue, and dinitrophenol, a powerful metabolic stimulant and oxidant. Their effectiveness clearly indicates the specificity of methylene blue, the high combining chemical efficiency of methemoglobin, and the subordinate importance of tissue oxidation, at least as activated by dinitrophenol.

5. Life tests for methemoglobin formation in certain species of animals are useless. There are procedures for and limitations of blood examinations which are valuable in interpreting and transferring results to human cases of poisoning.

A case of cyanide poisoning treated with **methylene blue (methylthionine chloride)** intravenously is reported by M. A. Walker (J. Kansas M. Soc. 35: 53 (Feb.) 1934) with recovery. The patient had drunk 60 c.c. (2 ounces) of a solution of sodium cyanide of an unknown concentration. Ten minutes after 50 c.c. (1½ ounces) of approximately 1 per cent solution of methylene blue had been injected intravenously, the patient was able to remonstrate against treatment. His pulse became slower and stronger. After 2 minutes, when 115 c.c. (3½ ounces) had been infused, the patient's skin was seen to be turning blue of a shade different from his previous observed cyanosis. After a hypodermic of **apomorphine hydrochloride**, about 500 c.c. (1 pint) of blue liquid with a strong odor of cyanide was vomited. The patient left the hospital 20 hours after admission, apparently well.

**DEXTROSE.**—*Administration.*—Dextrose *phlebotoclysis* is, in certain conditions, a life-saving measure. It would be a shocking revelation could statistics be collected as to the number of people who annually die from hypohydration of the system, when their lives might have been spared by the parenteral administration of 5 per cent. dextrose-saline solution, of the number of patients lost from hypochloridation when dextrose-saline phlebotoclysis might have prevented their death; the number of ketosis deaths that might not have occurred had dextrose been given; and the occasional life that might have been saved by osmotherapy. What is no less pathetic is that, in many instances, lives are lost in the conditions mentioned even though dextrose solution is administered, simply because the patient is not given enough, or because the remedy is not employed early enough, or because the solution administered is not of the proper composition.

The reasons are not far to seek. Dextrose infusion has been but recently introduced into the practice of medicine, and there may be some physicians who still consider it a passing new-fangled notion. Then there is the conviction that this is essentially a hospital procedure, entirely unsuited to medical practice in the home. Likewise, the idea exists that it is impossible to secure properly pre-

pared solutions in convenient containers for emergency administration in the home; and that there are inherent difficulties in the procedure itself requiring meticulous technic difficult to master. B. Fantus (J. A. M. A. 102:2165 (June 30) 1934) believes the rate of injection has a great deal to do with untoward reactions; and that the best way to prevent "speed shock" is by the drip method of administration, *i. e.*, that the individual drops be counted by means of a rectal drip bulb. Hypertonic solutions should be given more slowly than isotonic solutions. The solution in the container should, as a rule, be at 120° F. (48.9° C.) and the container surrounded by a hot-water bottle or similar device to maintain this temperature. It will lose from 15 to 30° F. before it is delivered into the vein. He believes:

1. In all very sick patients an adequate income of water, sodium chloride and dextrose should be taken care of as a routine procedure before rather than after a high degree of deficiency has occurred.

2. This, in cases in which adequate oral administration is impossible, can generally best be accomplished by dextrose phleboclysis, the composition of which should be determined by the individual indications present

3. For combating hypohydration and for the relief of thirst, 5 per cent dextrose solution in distilled water seems preferable

4. Whenever salt starvation is threatened or present, dextrose-saline phleboclysis should be practiced

5. Whenever carbohydrate cannot be ingested or digested to a sufficient degree, 10 per cent dextrose phleboclysis should be resorted to.

6. In poisoning with diffusible poisons, the diuretic and possible liver protective actions of dextrose phleboclysis adds itself to the foregoing therapeutic values

7. Concentrated (25 per cent) dextrose solution may be of value in certain internal hemorrhages, in inflammatory and exudative pulmonary edema, to lessen intracranial pressure (unless there is cerebral hemorrhage) and possibly in myocardial weakness.

8. During phleboclysis, other remedies may be conveniently infused, *e g.*, antisera, epinephrine, insulin, iodide, sedatives and stimulants

**Therapeutics.**—The use of dextrose in the treatment of *post-arsphenamine dermatitis* is shown by L. W. Shaffer (Arch Dermat and Syph 29 173 (Feb) 1934). It is difficult to evaluate the results, because the number of patients treated was not large and because cases of arsenical dermatitis vary greatly in the severity of manifestations and in the length of hospitalization. Results from the use of dextrose were encouraging and at times almost miraculous, so that such treatment has been continued. The use of dextrose in dilute solutions (from 2 to 10 per cent) as a diluent for arsphenamine has been recommended by several investigators to prevent arsphenamine reaction, as well as its use by mouth preceding the injection. Shaffer proposes to treat any new patient (non-diabetic) having accessible veins with 1 Gm (15 grains) of **sodium thio-sulphate** and 50 cc (1½ ounces) of a 50 per cent solution of **dextrose** injected intravenously daily for from 3 to 5 days. The administration of the dextrose should be followed in ½ hour by 5 units of **insulin**. Patients in whom venipuncture is difficult or impossible should be treated with **liver extract** by intramuscular injection or with **calcium gluconate** according to the saturation technic of Karrenberg. The usual supportive and local measures of treatment were employed.



The effect of dextrose in cardiac disease has been studied by A. E. Smith and D. Luten (*Am. Heart J.* 9:437 (Apr.) 1934). They report 16 cases of heart failure in advanced *heart disease* in which an opportunity was afforded for the comparison of the effects of dextrose and digitalis. In 9 cases, dyspnea was relieved to some extent by dextrose. The effect, however, was of short duration (from 3 to 12 hours) as compared with the more lasting effect of digitalis. Dextrose failed to restore compensation in any case. Digitalis restored compensation in 3 cases. The first injection of dextrose seemed to have a more beneficial effect than subsequent ones. According to the results, dextrose therapy appears to be indicated as an emergency measure in cases of acute or urgent heart failure and in cases of advanced chronic heart failure in which digitalis in adequate amounts has not restored compensation.

Hypertonic dextrose solution intravenously seems to have a special value in heart weakness with or without edema.

**DINITROPHENOL.—Physiological Action.**—There is no doubt that dinitrophenol can increase the tissue metabolism without producing the side actions that accompany metabolic stimulation by thyroid or thyroxine. W. C. Cutting and M. L. Tainter (*J. A. M. A.* 101:2099 (Dec. 30) 1933) showed that subjects excreted less nitrogen than they ingested; apparently body proteins are not broken down, although fats were completely burned by dinitrophenol; and it primarily promotes the burning of carbohydrates.

The oral administration to resting patients of sodium dinitrophenol in therapeutic doses, during short periods of time, caused no significant changes in vital capacity and in blood-pressure. There were significant increases in the pulse rate and in the venous pressure. These increases persisted during the medication and were maximum during the periods of peripheral vasodilatation caused by the drug in 13 cases of apparently normal cardiovascular system as studied by A. B. Stockton and W. C. Cutting (*Ibid.* (Sept. 22) 1934).

**Untoward Effects.**—A year has elapsed since the introduction of alpha dinitrophenol into therapeutics by M. L. Tainter, A. B. Stockton and W. C. Cutting (*Ibid.* 101:1472 (Nov. 4) 1933). On account of recurring toxic manifestations and allergic reactions, the necessity for skillful medical supervision has been recognized and repeatedly emphasized. A dinitrophenol prescription should be made non-refillable. The reasons are obvious, in view of the following case reports of poisoning in so short a time.

J. H. Masserman and Harry Goldsmith (*Ibid.* 102:523 (Feb. 17) 1934) report 1 death in a series of 18 patients between the ages of 18 and 40, free from discoverable organic disease, whose psychobiologic underactivity was evidenced by sluggishness, passivity and apathy. These patients were given 60 mg. (1 gram) of sodium dinitrophenol daily and the dose was increased 60 mg. (1 gram) every third day to a maximum of 5 mg. ( $\frac{1}{12}$  gram) per kilo ( $2\frac{1}{2}$  lbs.) in divided doses or until adverse symptomatology contraindicated further treatment. Six of the 18 showed some improvement in their further treatment. Toxic effects, characterized by fall in blood-pressure, tachycardia, acidosis and progressive stupor, were observed in 5 cases; in 1, death occurred.

F. E. Poole and R. B. Haining (*Ibid.* 102:1141 (Apr. 7) 1934) report 1 case where death followed the approximate ingestion of 2880 mg. (44 grams) taken in a period of 5 days. These capsules were bought from a druggist at the suggestion of a friend and taken according to directions on the label. Death resulted 7 days after beginning treatment. The dosage in this case was high but within the presumed limits of safety, so that the fatality should probably be regarded as an example of allergic idiosyncrasy.

M. L. Tainter and D. A. Wood (*Ibid.* 102:1147 (Apr. 7) 1934) give details of a case report (*Ibid.* 101:1333 (Oct. 21) 1933) in which a physician had taken 5 Gm. (1¼ dram) of the drug at one dose. Death occurred in 11 hours. The drug was self-administered with the apparent attempt to produce hyperpyrexia as a therapeutic measure for a supposed syphilis of the central nervous system.

An editorial (*Brit. M. J.* 1:539 (Mar. 24) 1934) referring to the recent death of a young professional dancer from poisoning by a nitrophenol compound, has given publicity to the dangers of taking allied compounds for the purpose of "slimming."

H. Dintenfass (*J. A. M. A.* 102:838 (Mar. 17) 1934) presents a case where there followed *impairment of hearing* 7 months after taking 20 grains (1.3 Gm.) in a period of 4 days. H. Jackson and A. I. Duvall (*Ibid.* 102:1844 (June 2) 1934) report a case which showed a generalized *erythematous papular eruption* over the whole body including the scalp, associated with marked *itching*. In this case there was a history of allergic reaction to horse serum.

N. Sidel (*Ibid.* 103:254 (July 28) 1934) observed the case of a woman, aged 26, who took approximately 360 mg. (24 grains) of dinitrophenol daily, for 2 weeks. *Urticaria* with *pruritus* developed, and subsequently intense *jaundice*, with an enlarged, tender liver and clay-colored stools. Gradual improvement is taking place, although she has been jaundiced 9 weeks to date.

*Neutropenia* following dinitrophenol was reported in a case observed by E. N. Davidson and M. Shapiro (*Ibid.* 103:480 (Aug. 18) 1934), with recovery, one by S. Silver (*Ibid.* 103:1058 (Oct. 6) 1934) followed by death, one by S. S. Bolin (*Ibid.* 103:249 (July 28) 1934) following ingestion of 21.8 Gm. (5½ drams) of the drug over a period of 4 months. G. M. Frumess (*Ibid.* 102:1219 (Apr. 14) 1934) stresses the fact that dinitrophenol produces *skin eruptions* in a large percentage (at least 7 per cent) of those to whom the drug is administered. These eruptions occur when nontoxic amounts of the drug are used. Some of the eruptions are definitely allergic, specific antibodies being produced in some individuals by the ingestion of the drug. In at least one case, these antibodies were demonstrable by the Prausnitz-Kustner passive transfer test. It is theoretically dangerous to resume the use of the drug after a skin reaction from its ingestion has subsided.

**DINITRO-ORTHOCRESOL.**—*Physiological Action.*—The effect of dinitro-orthocresol as a substitute for dinitrophenol are reported upon by E. C. Dodds and J. D. Robertson (*Lancet* 2:1137 (Nov. 18) 1933). They claim that it has a powerful action on the body, and consequently extreme caution must be exercised with administration. A *safe* dose that will cause a definite increase in

the basal metabolic rate would appear to lie between 50 and 100 mg. ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) daily, for a normal person; or from 0.5 to 1 mg. ( $\frac{1}{130}$  to  $\frac{1}{65}$  grain) per kg. ( $2\frac{1}{5}$  lbs.) of body weight. Under no circumstances should the compound be administered in such quantities as to raise the basal metabolic rate above +50, as otherwise grave discomfort and danger will result. It must, also, be borne in mind that neither the pulse rate nor the blood-pressure is of any value in assessing the basal metabolic rate, since the characteristic action of this compound is an increase in metabolism without a proportionate stimulation of the cardiovascular system, such as occurs with the administration of thyroxine. Any attempt to arrive at the basal metabolic rate by the use of Read's formula would give misleading results. It would appear, therefore, that the action of the drug should always be checked by determination of the basal metabolic rate. These experiments show that it is possible to maintain the metabolic rate at a figure from 30 to 50 per cent above normal without the appearance of any discomfort or toxic symptoms. It follows that, provided the diet is not grossly in excess of the individual's requirements, weight will be lost, and it is possible to adjust the intake so that this loss will be constant. This will be possible without undue privation. As judged, it would appear that dinitro-orthocresol is about 5 times as potent as the dinitrophenol compound.

**Poisoning.**—E. L. Bortz, A. Sindoni, Jr., and E. M. Hobson (Pennsylvania M. J. 38:170 (Dec.) 1934) report 1 case in which 50 mg. ( $\frac{3}{4}$  grain) of dinitro-cresol was given over a period of 8 days, when the patient developed *jaundice* and pain in right upper quadrant of the abdomen. The icteric index was 12.6.

**EPHEDRINE.—Untoward Effects.**—It is pointed out by R. N. Chopra and B. Mukherjee (Indian M. Gaz. 68:622 (Nov.) 1933) that their studies indicated that toxic manifestations and undesirable side effects are commonly encountered after the use of ephedrine in asthma and other conditions. Ephedrine in doses of from 1 to 10 mg. ( $\frac{1}{65}$  to  $\frac{1}{6}$  grain) per kg. ( $2\frac{1}{5}$  lb.) of body weight is known to cause a rise in the blood-pressure of anesthetized dogs by 100 or more millimeters of mercury, and the rise is maintained at this level for at least 15 to 25 minutes. In human beings the rise in pressure is not so high as in animals, but it varies from 20 to 65 mm. of mercury. It is easy to see that circulatory reactions, such as palpitation and anginal pain, will be produced by the drug, particularly when the systolic pressure is at its highest level. The symptoms are also found to disappear as the pressure returns to normal. Insomnia and tremors are possibly due to stimulation of the central nervous system. Constipation, nausea and anorexia may be explained by the paralytic condition of the intestine, due to sympathetic stimulation and loss of tone. Headache and throbbing sensations in the temples may be attributed to changes in pressure in the arterioles or veins within the skull. There is no agreement regarding the dosage required to produce these effects. Ephedrine is undoubtedly not a very toxic alkaloid and consequently there is a wide margin of safety. Its minimal lethal dose when given intravenously in dogs was found by Chen to be from 70 to 75 mg. ( $1\frac{1}{10}$  to  $1\frac{1}{6}$  grains) per kg. ( $2\frac{1}{5}$  lbs.) of body weight. From this it may be inferred that a man weighing from 50 to 60 kg. (110 to 132 lbs.)

would require from 4 to 5 Gm. (1 to 1¼ drams) of the alkaloid to produce a fatal result. In contrast to this, the usual therapeutic dose is from ½ to 2 grains (0.03 to 0.13 Gm.), and 7 grains (0.45 Gm.) have been given in a single dose without untoward effects. The only explanation of the toxic effects appears to be a state of hypersensitiveness of certain persons to the drug. Ephedrine is a sympathomimetic drug and the stimulation of the sympathetic system in a highly-strung individual may lead to symptoms of sympathoparasymphathetic imbalance. It is also well known that slight differences in the amount of calcium in the blood make the autonomic system sensitive to sympathomimetic drugs, of which ephedrine is one. If during its administration the patient exhibits toxic symptoms, the drug should be discontinued.

**Therapeutics.**—A. R. Gilchrist (Brit. M. J. 1·60 (Apr.) 1934) observed that ephedrine, taken orally, increased the ventricular rate in 4 out of 6 cases of *complete heart block*. In 2 cases the test was indecisive. Barium chloride produced no demonstrable effect on the ventricular rate in the 4 cases responding to ephedrine. It did no harm in doses larger than those originally recommended. In 2 cases of complete heart block, complicated by occasional Stokes-Adams seizures, ephedrine taken for 2½ and 1½ years proved entirely successful in the prevention of syncopal attacks. When the drug was discontinued, typical seizures returned. Gilchrist recommends that the dose of ephedrine should be the minimal quantity consistent with an acceleration of the resting ventricular rate, a larger dose may cause overstimulation. If the drug is then omitted suddenly, profound slowing of the ventricular rate, with repeated Stokes-Adams attacks, may occur as a result, presumably, of exhaustion of the idioventricular center. A dose of ½ grain (0.03 Gm.) by mouth at intervals of 8 hours may be sufficient.

In view of the constantly increasing frequency of *serum disease*, P. P. Levy (Presse méd. 41 1906 (Nov. 25) 1933) recommends the ingestion of ephedrine before the injection of serum and at regular intervals afterward for the *prevention* of serum accidents. He considers it superior to epinephrine because it is efficacious when ingested and its action is slower, more gentle and more lasting. The first tablet of ephedrine is ingested 1 hour before the injection of the serum, and thereafter a tablet is taken every 8 hours (even during the night) for 14 days. For children aged from 1 to 4 years, tablets of 0.01 Gm. (⅙ grain) are used, for children aged from 4 to 9, tablets of 0.02 Gm. (⅓ grain), and for patients of more than 9 years, tablets of 0.03 Gm. (½ grain). In a grave case of diphtheria in which a delay of 1 hour before serum injection is considered dangerous, a solution of ephedrine containing the equivalent of the tablet may be injected parenterally 20 minutes before the serum injection. This method of prophylaxis has been tried in a number of patients, ranging in age from 18 months to 55 years, who received intramuscular or subcutaneous injections of nonpurified antidiphtheritic serum in doses varying from 10 to 500 c.c., spread over several days. Among 78 children receiving this treatment, 5 experienced marked reactions, with strong or average eruptions and general symptoms, while 14 had only slight eruptions without general symptoms and 59 had no reactions at all. Among 39 adults receiving the same treatment, 8 experienced strong

reactions while 31 experienced no reaction or only slight cutaneous eruptions without general symptoms.

**GASOLINE AND KEROSENE.—Poisoning.**—A summary of the clinical and laboratory examinations in 7 cases of gasoline poisoning and 65 cases of kerosene poisoning, admitted to one hospital between October, 1931, and July, 1933, is given by J. A. Munn and F. M. Martin (J. A. M. A. 103:472 (Aug. 18) 1934). The ages were between 18 months and 4 years. There was a mortality of 9.2 per cent. in the kerosene cases and 28 per cent. in the gasoline cases. The toxicity produced by the ingestion of coal oil or gasoline need not cause the great concern that aspiration or inhalation of these hydrocarbons cause. It was the patients who aspirated as well as ingested one of these petroleum products who presented a much graver clinical picture, owing to the rapid development of pneumonitis.

In the *treatment*, it was recommended to remove as much of the offending agent as possible, by **gastric lavage** or **emesis** and **laxatives**. During gastric lavage there is much retching, struggling and breath catching, which seems to favor aspiration of stomach contents into the lungs. There is less likelihood of aspiration of the fluid when emesis is produced by the oral administration of **syrup of ipecac** than when gastric lavage is employed. In more recent cases when *cyanosis* and other signs of respiratory embarrassment are present, it was found that the use of **oxygen** (95 per cent.) and **carbon dioxide** (5 per cent.) has been of considerable benefit. Therefore, the administration of oxygen and carbon dioxide in all cases that show such signs is suggested. It is employed for its stimulating action on the respiratory center rather than to increase the oxygen-carrying power of the blood. **Atropine sulphate** and **caffeine sodiobenzoate** are recommended hypodermically for their stimulating effect.

**GELATIN.—Therapeutics.**—Sheet gelatin for the treatment of *muscular dystrophy* and other similar disorders, is cheap, and contains from 15 to 20 per cent of glycine. The gelatin, 100 Gm (3½ ounces), is emulsified in orange or pineapple juice and given to the patient as a daily ration, to be taken at his convenience during 24 hours. The cases treated by L. Stone and M. M. Abeles (J. Nerv. and Ment. Dis. 80:285 (Sept.) 1934) were of long standing, probably much less amenable to any form of therapy than incipient cases. Nine exhibited subjective sensory phenomena. Of these, 5 showed *muscular dystrophy*, 1 *myasthenia gravis*, 1 *amyotrophic lateral sclerosis*, 1 *progressive muscular atrophy*, and 1 *chronic anterior poliomyelitis*. After treatment, 9 patients felt subjectively stronger to varying degrees. Eight showed an increase in muscular strength, omitting the myasthenic patient, who may have had a spontaneous remission. The changes varied in degree; they were all slight and 2 were altogether questionable. It is believed that the clinical phenomenon is sufficient to indicate that the substance has some therapeutic potency, which is possibly more marked in incipient cases. The therapeutic effect is probably due to the glycine content. The gelatin is bulky and unpalatable, and the results do not indicate superiority over pure glycine. Nevertheless, it might be the subject of further experiment in an effort to provide an inexpensive source of glycine. The pres-

ence of sensory phenomena and even slight motor improvement in cases other than primary muscular dystrophy suggests that there may be similarities, perhaps identities, between the primary disorders of muscle metabolism and those of neurogenic origin, and that some aspects of the latter disorders may therefore be influenced favorably by glycine.

**GLYCERIN.**—*Therapeutics.*—F. Lickint (Munchen med Wchnschr. 81:821 (June 1) 1934) points out that the great increase in the incidence of *renal* and *ureteral calculi* has augmented the demand for conservative remedies. After evaluating ureteral massage, dilation of the ureters, increased flooding of the urinary passages by the administration of large amounts of fluid, hypophyseal preparations for the stimulation of peristalsis, and the use of volatile oils, the article discusses the part of glycerin in normal metabolism; the elimination of glycerin following its administration; and its mode of action in expelling calculi. It calls attention to its spasmolytic action, with its stimulating effect on the peristalsis by withdrawal of water or by reflex action from the intestine to the ureters; its diuretic action; its lubricating action; the increased density and viscosity of the urine; and the facilitation of expulsion by dissolving and diminishing the calculi. Small doses will result in failure, and at least 50 c. c. (1½ ounces) of glycerin 3 times daily for 3 successive days must be given. Undesirable effects have never been observed after the administration of glycerin. Expulsion of the stone in 14 out of 16 patients to whom the dose mentioned was given was obtained.

**GLYCINE.**—*Therapeutics.*—The idea of treating *muscular dystrophy* by the administration of glycine resulted directly from chemical analysis of the urine. The fact that the method is not yet definitely established as clinically successful in the present form of application does not detract from the essential importance of the fundamental observations. Creatinuria has been noted in many diseases that primarily or secondarily attack the muscular system. This led Thomas and his coworkers to investigate the effect of prolonged administration of glycine on the clinical course of progressive muscular dystrophies. With the decrease in the creatinuria there was a rise in the creatinine output and an improvement in the patient's ability to hold ingested creatine. It was also reported that simultaneously the patients improved clinically.

D. P. Cuthbertson and T. K. MacLachlan (Quart J Med 3:411 (July) 1934) recently reported the results of prolonged glycine administration in 9 cases of muscular dystrophy of different types and in 2 other cases exhibiting selective muscular atrophy. These patients were placed on a basal diet free from meat, meat extract and fish. The total creatinine and preformed creatinine outputs were estimated in the 24-hour specimens of urine. The difference between the two estimations represented the quantity of creatinine excreted. At various intervals the patient's reaction to ingested creatine was determined. During these periods no glycine was taken. The amounts excreted were expressed as milligrams of nitrogen daily. Glycine therapy was usually started about 3 or 4 days after the first dose of creatine. The adults received 15 Gm (½ ounce) daily; the children, 10 Gm. (2½ drams) daily, dissolved in milk. Generally speaking,

the greater the muscular incapacity, the greater the degree of creatinuria and the less the excretion of creatinine.

Clinically, 5 of the 9 cases of muscular dystrophy were of the pseudohypertrophic type. With one exception, the cases belonging to the dystrophy group showed definite general improvement, as evidenced by increase in weight, gain in strength and feeling of wellbeing. None of the patients became worse. In the majority there was also some evidence of improvement in the power of some of the specific muscles affected, but this was least in the pseudohypertrophic group. The Glasgow workers believe that in the majority of the cases the changes were in excess of those which might be expected to occur from hospitalization alone, but that the term "cure" cannot be applied to the end-results.

In another investigation on the same subject, F. Linneweh and W. Linneweh (Deutsches Arch. f. klin. Med. 176: 526 (July 9) 1934) attempted to study the question of possible glycine deficiency in *muscular dystrophy*. Their work was based on the studies of Magnus-Levi, Lewinski and Quick, which demonstrated that a portion of benzoic acid, when ingested in large doses, is excreted as glyconic acid monobenzoate instead of quantitatively as hippuric acid, and that the appearance of this reducing substance in the urine is a sign of glycine poverty of the organism. Two patients with unquestionable progressive muscular dystrophy and one normal person were investigated in this manner under controlled conditions of diet. The glycine supply and the glycine building power of the body were thus determined by the benzoic acid tolerance and it was established that no difference from the normal organism existed in this respect; therefore, no true glycine deficiency exists. Consequently, glycine therapy is not a form of substitution therapy and its mode of action remains uncertain.

Careful chemical and clinical studies are gradually clarifying the underlying scientific and practical applications of an undoubted consistent chemical abnormality (J. A. M. A. 103: 1236 (Oct. 20) 1934)

Two cases of *myasthenia gravis* which showed definite clinical improvement on a combination treatment of **ephedrine sulphate and glycine**, are reported by E. O. G. Schmitt (Ann. Int. Med. 7: 948 (Feb.) 1934). The administration of glycine was accompanied by an increase in the elimination of creatinine and preformed creatinine nitrogen. A dosage of 15 Gm ( $\frac{1}{2}$  ounce) twice daily of glycine is an effective dosage and probably the optimal. Ephedrine sulphate seems to augment the efficacy of the glycine; in the dose of  $\frac{3}{8}$  gram (0.024 Gm) twice daily given about 20 minutes after the dose of glycine.

W. M. Boothby (Arch. Int. Med. 53: 39 (Jan.) 1934) states that of 12 patients suffering from *myasthenia gravis* treated with ephedrine and glycine, 10 have shown definite improvement, and 4 of these have shown marked improvement. Two did not respond to treatment except that the progress of the disease was apparently arrested, one of the two died from causes not directly attributable to the myasthenic syndrome. By the careful use of either ephedrine or glycine, and more often of the two, the condition of most patients having *myasthenia gravis* may be improved sufficiently to permit them to return to work or at least to enjoy a useful life. Time alone will tell whether this improvement can be maintained. The disease occurs much more frequently than is generally supposed.

S. Kostakow (Deutsches Arch. f. klin. Med. 176:467 (July 9) 1934) discusses the value of glycine in the treatment of *progressive muscular dystrophy*. His observations were made in 16 cases. A tabular report of the results of the treatment indicated that the degree of improvement and the responsiveness of the disorder are dependent on the length and the progressiveness of the disorder but not on the age of the patient. The impression gained is that the degree of improvement is proportional to the extent to which the muscles are still capable of reacting and inversely proportional to the progressiveness and the duration of the disorder. He rejects the statement that children with progressive muscular dystrophy are not at all or only slightly influenced by glycine, because his observations on 7 children who improved greatly disprove this. He admits, however, that glycine is ineffective in cases with myasthenic components or with degenerative atrophies in syringomyelia, in spinal forms, and in bulbar paralysis. Glycine treatment is indicated in pure myopathy and, to a certain extent, in cases in which on the bases of the clinical and electrical behavior serious impairment of the peripheral neuron can be excluded. He emphasizes that active patients require much larger quantities of glycine than do patients who rest.

The effects of glycine feeding have been studied in 9 cases of progressive muscular dystrophy for periods up to 14 months. Little tangible evidence of improvement in muscular function has been obtained (J. G. Reinhold, J. H. Clark, G. R. Kingsley, R. P. Custer and J. W. McConnell. J. A. M. A. 102:261 (Jan. 27) 1934).

Muscle specimens removed at biopsy after treatment were distinctly better in quality, chemically and histologically, than similar specimens taken before treatment. Restoration of various characteristic muscle components accompanied regeneration of the muscle fibers.

High protein diets, beef extract and gelatin proved to be helpful supplements to glycine. Ephedrine has been of value in one case.

A patient with *generalized chronic myositis* that closely simulated the clinical picture of muscular dystrophy showed considerably improved muscular function following glycine therapy.

Despite the marked improvement in the structure and composition of the muscles in *progressive muscular dystrophy* after treatment with glycine (as indicated by examination of the biopsy specimens), a great disparity with the normal remained, probably sufficient in many cases to account for the failure of muscular function to be restored to a greater extent.

**HISTAMINE.—Therapeutics.**—Histamine has been recommended by a number of authors in the treatment of fibrositis, neuritis, and in all chronic rheumatic disturbances associated with pain and limitation of movement.

F. S. Mackenna (Lancet 1:1228 (June 6) 1934) presents the results he has obtained in *rheumatism* with histamine by ionization and massage. With the treatment, the patient experiences an immediate relief from pain, either complete or partial, and can demonstrate a greater range of movement when previously there was restriction. This lessening of pain is always present and may last a few hours, a few days or permanently. In addition, there is a feeling of local



warmth and general wellbeing. The undesirable results that must be carefully watched for, include headache, or a feeling of fullness in the head; tachycardia; a feeling of constriction in the chest with consequent breathlessness; burning and faintness; any one of which is an indication for the immediate cessation of the treatment. Treatment may be given daily. Histamine has a definite place in the treatment of *fibrositis*, *neuritis*, and in all *chronic rheumatic disturbances* associated with pain and limitation of movement. With histamine it is possible to cure fibrositis and neuritis completely and almost invariably.

B Shanson and C. G. Eastwood (Lancet 1: 1226 (June 9) 1934) studied the effects of histamine in the treatment of 70 adult cases of *chronic rheumatism* and allied disorders. The series included examples of *rheumatoid arthritis*, *fibrositis*, *osteoarthritis*, *subacute rheumatism* and *gout*. Histamine was given by subcutaneous injection. The solution was prepared in the strength of 1 mg. ( $\frac{1}{65}$  grain) of histamine acid phosphate to 1 c.c. (16 minims) of saline solution, and 0.5 per cent. phenol was added as a preservative. The initial dose was 0.1 mg. ( $\frac{1}{600}$  grain), *i. e.*, 0.1 c.c. ( $1\frac{1}{2}$  minims), and this was increased daily by 0.05 mg. ( $\frac{1}{1200}$  grain) until definite improvement was observed. A satisfactory dose was usually found to lie between 0.1 ( $\frac{1}{600}$  grain) and 0.5 mg. ( $\frac{1}{120}$  grain). This dose was repeated twice or 3 times a week and further increased if the response diminished. The response to histamine varied from patient to patient, and even in the same patient at different times. The following is a list of all the effects that were observed: flushing, relief of pain, increased range of joint movement, relief of vasomotor symptoms, sweating, headache, dizziness, drowsiness, increased appetite, a sense of wellbeing, changes in blood-pressure and temperature, and paresthesias.

P. H. Kling (Am J Surg. 99: 568 (Apr.) 1934) states that the alteration of the peripheral circulation is the principle underlying the treatment of rheumatic conditions and disturbances of the vasomotor system by the application of histamine to the affected parts. The effect of this treatment consists in a dilatation of the minute vessels and smaller arterioles and in an increase of the blood flow and permeability of the vessels, which causes a hyperemia and elevation of the skin temperature for several hours. A definite conclusion of the value of this method is at present possible only in myalgia (myositis). Of 20 cases of *myalgia*, 18 were cured or improved and 2 remained unchanged. Immediate relief of pain and tenderness after the first treatment is a favorable prognostic indication in this group. Secondary myalgia, after trauma, strain, and due to static unbalance was benefited in a moderate number of cases.

**IODINE.—Therapeutics.**—Iodine is still given indiscriminately to any type of goiter. It is, however, of generally recognized value in the prevention of development of *endemic goiter*: (1) for the prophylaxis, only minute quantities are necessary, a small dose of  $\frac{1}{6}$  grain (0.01 Gm.) of iodine per week; and (2) in the management of *hyperthyroidism preparatory to operation*. H. M. Clute and L. S. Pilcher, II (New England J. Med. 210: 117 (Jan. 18) 1934) emphasize that iodine does not cure hyperthyroidism. The long-continued admin-

istration of iodine in hyperthyroidism increases the risk of surgery by prolonging the duration of the hyperthyroidism.

H. K. Ransom and R. H. Bayley (West J. Surg. 42:464 (Aug.) 1934) claim that iodine should be reserved for the period of preoperative preparation, as its long-continued use deprives the patient of an induced remission prior to operation. Too many patients with hyperthyroidism are still being treated with iodine alone.

Delay in surgical intervention as well as iodine-drugging are among the most important factors in accounting for unexpected postoperative disasters. Iodine may be used safely in the preoperative preparation of all types of goiter.

However, S. F. Haines (*Ibid.*, p. 449) controls *recurrent* or *persistent exophthalmic goiter* occurring after one or more resections of the thyroid by iodine alone so well that further surgical procedures were not advised. None of the patients who received iodine for long periods suffered any deleterious effects that could be ascribed to its use. It is not assumed that the effect of iodine was curative, but only that in the cases observed, the manifestations of the disease were controlled during the time of administration of iodine.

The experiments of A. Strickler (Arch. Dermat. and Syph. 28:836 (Dec.) 1933), in developing a formula for the local treatment of *epidermophytosis*, indicate that potassium iodide appears to possess the property of enhancing the fungicidal power of vaporized iodine. A 3 per cent. dilution of **salicylic acid** and a 20 per cent. dilution of **benzoic acid** seem capable of increasing the fungicidal properties of **vaporized iodine** to a slight degree. **Boric acid** was found capable of assisting vaporized iodine slightly. The control experiment with talc alone seemed to show that this substance does not possess any fungicidal or fungistatic properties. However, it may act as an additional barrier and it may be prudent in future chemotherapeutic investigations to use this or some other inert powder so as to more closely simulate experimentally the nonpenetrating mechanism of the human horny layer. The following local application for *epidermophytosis* is proposed: 1.3 Gm. (20 grains) of **iodine crystals**, 1.9 Gm. ( $1\frac{1}{2}$  dram) of **potassium iodide**, 1.9 Gm. ( $1\frac{1}{2}$  dram) of **salicylic acid**, 3.8 Gm. (1 dram) of **boric acid** and enough of 50 per cent. **alcohol** to make 59.1 cc. ( $1\frac{9}{10}$  ounces). This preparation is applied as a paint once or twice a day. It has been used for months in a dermatologic clinic.

**INSULIN.—Therapeutics.**—The uses of insulin in various conditions other than diabetes have been many and varied. A few additional indications are added, as follows:

W. L. Sharp and M. A. Bahr (J. Indiana M. A. 27:210 (May) 1934) studied the effect of insulin therapy in 3 cases of *dementia precox* (2 of the catatonic and 1 of the simple type), 1 case of *involutional psychosis*, and 1 of *manic-depressive psychosis* in the depressed phase. Three of the patients were eating but little and 2 were on actual hunger strikes. All of the cases were thin and emaciated. The insulin was given 3 times daily in 10 unit doses, 30 minutes before meals, and no change was made in the routine of the patients. Definite increases in weight and strength were noted after 4 weeks of insulin therapy, but some of this was lost in the 2 months following the cessation of the treatment.

It is believed that this was due to the mental states, *viz.*, negativism in the 3 precox cases and the depressed, melancholic state in the cases of involutional psychosis and manic-depressive psychosis. X-ray examination of the gastrointestinal tract tended to show some improvement in the emptying time of the stomach and colon. However, the results were not striking. The mental state improved only in the manic-depressive patient.

*Hyperinsulinism* was treated by H. J. John (Endocrinology 17: 583 (Sept.-Oct.) 1933) with small doses of insulin (10 units) after meals with a view to forestalling discharge of that hormone by the pancreas. The results were notably favorable. Whether or not 10 units of insulin 3 times a day is the optimal dosage has not yet been determined. Perhaps a gradual increase to the point of tolerance might prove more effective in some cases.

C. R. Jones (Am. J. Digest. Dis. and Nutrition 1: 135 (Apr.) 1934) notes that in treating patients with *peptic ulcer* in recent years, he has made a point of building up the general health, and in undernourished patients has often used insulin to obtain an improvement in the carbohydrate metabolism and a gain in weight. In these cases, it was noted that in addition to this improvement, the ulcer pains grew less and finally disappeared, and there was definite evidence of healing of the ulcer. In most of the cases treated, the dose was from 10 to 15 units of insulin (occasionally 20 units) twice a day, 15 minutes before each of the 2 main meals of the day, 100 Gm ( $3\frac{1}{8}$  ounces) of mashed potato must be taken at each of these meals. In uncomplicated cases of fresh peptic ulcer and recurrent peptic ulcer, decrease in pain and improvement in subjective symptoms begin to be evident after a few days of treatment. In 2 to 3 weeks symptoms are completely relieved, and x-ray signs of ulcer have disappeared. With insulin treatment, diet is less restricted than the usual ulcer diet; liquid diet is not required for more than a week, then, semi-solid food; and, finally, a solid food diet avoiding rough and irritating foods.

Insulin was used as a means of attempting *suicide*, in a diabetic case reported by J. T. Beardwood (J. A. M. A. 102: 765 (Mar. 10) 1934). The amount taken was 390 units of insulin in 15 minutes and the case came under control  $\frac{3}{4}$  hour later. On admission the blood sugar was 64 mg. Treatment by **intravenous dextrose solution** was followed by recovery.

**IRON.—Therapeutics.**—The effects of treatment with simple iron preparations of 42 cases of *iron-deficiency anemia*, 28 with achlorhydria, are shown in tabulated form by F. H. Bethell, S. M. Goldhamer, R. Isaacs and C. C. Sturgis (J. A. M. A. 103: 797 (Sept. 15) 1934). These results compare favorably with those reported by others employing combinations of iron with other substances, in the treatment of the same type of anemia.

Relatively large amounts of ingested iron are required for satisfactory clinical and hematologic improvement. **Ferrum reductum**, 15 Gm (23 grams) daily, or **ferric ammonium citrate**, 4 Gm (1 dram) daily, administered in 3 divided doses after meals, is therapeutically optimal. Following the institution of treatment, a latent period, during which no change in the peripheral blood picture occurs, is attributed to the time required for maturation by the primitive erythro-

cytes in the bone marrow. In general, the blood of patients with acid gastric secretion responds more promptly to iron medication, and a smaller dosage of the element is required than is the case of those with achlorhydria. In both groups the erythrocyte and hemoglobin values are usually restored to normal after from 6 to 8 weeks of therapy. Patients with achlorhydria often require continued treatment with iron in order to prevent recurrence of anemia.

Administration of highly purified ferrum reductum in conjunction with a "low copper" diet did not detract from the efficacy of the iron, as evidenced by the rate of hemoglobin formation.

J. K. Everhart (Pennsylvania M. J. 37:474 (Mar.) 1934) states that the average infant and young child will tolerate from 10 to 20 grains (0.65 to 1.3 Gm) of iron and ammonium citrate daily. It is readily soluble and may be given in the infant's milk and is not likely to cause disturbance. When hemoglobin has reached abnormally low levels, a considerable period of time is often noted before marked improvement follows. Continuous treatment for several months should be the rule. At times, it is advisable to change the preparation to another iron salt.

W. P. Murphy (Ann. Int. Med. 7:939 (Feb.) 1934) believes iron as ferrous carbonate or ferric ammonium citrate is more effective than as ferric citrate in *secondary anemia*. Liver and iron given together produce better results than when either is given separately. *Ferrous carbonate* (U. S. P.) in daily amounts of 4 Gm (1 dram) and *ferric ammonium citrate* (U. S. P.) 3 Gm ( $\frac{3}{4}$  dram) are sufficiently large doses. The improvement of the blood and of the patient's general condition may be hastened by an intramuscular injection of 3 c.c. ( $\frac{3}{4}$  dram) of **concentrated liver extract** at intervals of 5 to 7 days.

Due to the large doses of iron salts necessary to administer sufficient of the usual preparations—iron and ammonium citrate, 10 Gm ( $2\frac{1}{2}$  drams) daily and Bland's pill in dose of 45 to 60 grains (3 to 4 Gm) daily—H. W. Fullerton (Edinburgh M. J. 41:99 (Feb.) 1934) suggests the use of **ferrous sulphate** in small doses (9 grains—0.58 Gm—daily). He treated 21 cases of *hypochromic anemia* with small doses of ferrous sulphate in tablet form. Ten patients (48 per cent) showed an average daily hemoglobin increase of 1 per cent or more and accordingly may be regarded as having responded satisfactorily to this form of therapy. Three patients showed a good response, although falling short of the standard rise of 1 per cent hemoglobin a day. The remaining 8 cases were complicated by hemorrhage during treatment. A comparison of the efficacy of iron preparations in the treatment of hypochromic anemia has shown that ferrous sulphate treatment appears to be reliable when hemoglobin deficiency is the essential feature and that the speed of its return to normal is surely the best index of therapeutic efficiency. [The reviewer has used this preparation in 2 cases of hemorrhage of peptic ulcer with excellent results.]

**LEAD POISONING.**—Lead colic and bilateral wrist-drop have long been recognized as the classic symptoms of lead poisoning. Although lead has been regarded by many writers as the most important of the industrial hazards leading to a special disease, the incidence of industrial lead poisoning is declining.

Lead is widely distributed in nature so that plants grown in soils that contain the element may acquire lead. The spraying of fruits and vegetables with insecticides is suggested as another probable source. Thus, it finds its way insidiously into the body in food. The average amount of lead in the feces of normal individuals with no undue exposure to lead was found to be approximately 0.03 mg. per gram of ash, by R. A. Kehoe, F. Thamann, and J. Cholak (J. Indust. Hyg. 15:257 (Sept.) 1933). The same investigators have shown that the presence of lead in urine to the amount of 0.02 mg. per liter is the rule and not the exception. Lead has been found in the cerebrospinal fluid of every individual known to be suffering from lead poisoning by I. M. Rabinowitch, A. Dingwall, and F. H. Mackay (J. Biol. Chem. 103:707 (Dec.) 1933).

Realization by physicians of the dangers to children of the continued ingestion of lead and dissemination to mothers of information on the subject should result in the prevention of the disease, according to C. F. McKhann and E. C. Vogt (J. A. M. A. 101:1131 (Oct 7) 1933). Lead deposited in the organs of the body may induce the symptoms referable to the various systems, but lead deposited in the bones is in an inert form. Thus, in relieving lead poisoning measures are usually recommended which tend to hasten the removal of lead from the circulation and the deposition of the metal in the bones. **Calcium salts or phosphates** diminish the solubility of lead in the blood and **viosterol** hastens the growth of bone. Removal of lead from the body may be accomplished by inducing an acidosis or an alkalosis, by deprivation of calcium or by the administration of **parathyroid extract**. Although the danger of the return of the symptoms of lead poisoning persists for some time, it gradually subsides, owing to the spontaneous elimination of the metal.

**LIVER THERAPY.**—During the past year investigators have shown that in *pernicious anemia* liver extract is much more potent, gram for gram, if injected intravenously or intramuscularly than if given by mouth. The injection treatment should replace transfusions unless the patient is *in extremis*.

P. W. Kinskern and L. G. Christian (J. Michigan M. Soc. 33:373 (July) 1934) present 9 cases of *pernicious anemia* which were treated with parenteral liver extract. Five were treated intravenously, 4 intramuscularly. All showed good response in blood regeneration. The two routes were not compared by giving identical doses, but the extract seems to be approximately as active when given either way. In 2 cases there was rapid response to intramuscular treatment after moderate oral doses of extract had failed.

During remissions, treatment should be an individual problem in each case. Large or frequent treatments are not, as a rule, necessary, but every patient should have frequent blood counts.

There is little evidence that treatment improves spinal cord changes, but where symptoms are present, special care should be taken to keep the blood up to normal in an attempt to arrest the combined sclerosis.

It is felt that the aim of treatment is to maintain a red cell count of 5,000,000; this can usually be accomplished with injections of extract equivalent to 100 Gm (3½ ounces) every 3 to 4 weeks.

O. Richter, A. E. Meyer, and A. C. Ivy (Ann. Int. Med. 7: 353 (Sept.) 1933) treated 21 patients having *pernicious anemia* and induced complete blood remissions in 3 of these cases by the intravenous administration of the equine liver extract. From 2 to 4 c.c. (1 c.c. prepared from 10 Gm of liver) of the material was injected at intervals of from 1 to 3 days. In 1 patient having a low blood count, with an initial hemoglobin of 24 per cent. and a red cell count of 840,000, a mild systemic reaction was occasionally noted following the rapid injection of liver extract. This consisted of an immediate drop in blood-pressure, accompanied by a rapid, weak pulse and dyspnea, followed later by a generalized feeling of warmth. This systemic reaction was usually absent when the liver extract was injected slowly, *i. e.*, less than 1 c.c. per minute. No serious reactions were observed among 60 intravenous injections. One of the three patients, previously resistant to treatment with large amounts of oral liver extract and whole liver, made a complete hematologic remission in 57 days on intravenous injections of equine liver extract. Equally good responses were obtained from subcutaneous and intravenous injections. Twenty-four patients suffering from relapses were treated with daily injections of subcutaneous horse liver extract. The average dose used was 2.5 c.c., containing the active principle of 25 Gm of horse liver. Patients entering the hospital in a semi-comatose or moribund condition received 2 or 3 injections (from 59 to 75 Gm—2 to 2½ ounces) daily until evidence of a reticulocyte response was obtained, and then once daily until the hemoglobin and red cell counts became normal. The maximal reticulocyte response was obtained between the fifth and seventh day and varied in this series of cases from 16.8 to 47.2 per cent. The average of the entire group was 27.6 per cent., omitting the patients who received previous therapy which had absorbed the maximal reticulocyte peak. A complete hematologic remission was produced in intervals of from 4 to 8 weeks and the majority of the patients treated showed an average daily gain of 1 per cent. hemoglobin and 57,194 red cells from the average daily injection of 2.14 c.c. of equine liver extract.

**MAGNESIUM CHLORIDE.**—*Therapeutics.*—R. H. Craig (Canad. M. A. J. 31: 531 (Nov.) 1934) cites a case where operation under tribromethanol and chloroform anesthesia disclosed a diffuse cancerous infiltration and edema of the larynx involving the epiglottis, the aryepiglottidean folds, the arytenoids, the true and false vocal cords, the subglottic spaces and the trachea as far down as the tracheotomy wound. There was some improvement in the patient's general condition following the operation, which was attributed to the removal of the septic foci, but, in spite of daily dressings and meticulous care, the laryngeal picture remained about stationary. The patient's condition was grave and the prognosis gloomy. As a last resort, magnesium chloride was administered (a) subcutaneously, (b) combined with pepsin as a spray for the pharynx, (c) with pepsin and glycerin as a dressing in the laryngeal cavity. The infiltration began to subside after the tenth treatment. The tracheotomy wound, which had been moth eaten and succulent in appearance, was now firm and healthy looking, the granulations in the laryngeal opening were white, healthy and glistening. The odor and cough had almost disappeared. The improvement

was pronounced and, in order to hasten recovery, magnesium chloride was prescribed by mouth. Two days later the man developed general malaise, with loss of appetite, and the tracheotomy wound had lost its healthy appearance. The magnesium chloride was discontinued and a purge of mild mercurous chloride was given. Forty-eight hours later he again felt comfortable and the appearance of the mucosa of the larynx and the tracheotomy wound gave the clue to the amount of magnesium chloride that could be tolerated and assimilated by the patient. Fifteen days after the treatment was begun the feeding tube was removed and deglutition returned gradually to normal. One month later the edema had disappeared from the epiglottis and the ulceration of the mucous membrane of the larynx had disappeared. When the tracheotomy tube was removed, the patient could whisper; abduction and adduction were returning slowly. One month and two days from the time the treatment was first started, the patient left the hospital.

**MAGNESIUM SULPHATE.**—*Physiological Action.*—The effects of ingestion of an ordinary purgative dose of magnesium sulphate on the plasma magnesium and the general physical condition in a series of patients suffering from renal disease, were studied by A. D. Hirschfelder (J. A. M. A 102: 1138 (Apr 7) 1934). In all these patients a tremendous rise in plasma magnesium occurred within 4 to 6 hours after an ordinary purgative dose of magnesium sulphate had been taken by mouth. While one such dose was not sufficient to raise the magnesium concentration in the plasma to the level at which coma set in, it often did rise to about two-thirds of the concentration, and a number of patients did show a decided increase of drowsiness or even a slight coma accompanying the increase in plasma magnesium.

Hirschfelder concludes as follows.

1. When normal individuals take Epsom salt by mouth, they excrete about 40 per cent of the ingested magnesium in the urine in 24 hours, but the concentration of magnesium in the blood plasma does not rise appreciably.

2. The concentration of magnesium in the plasma may vary greatly under clinical conditions.

3. There is a clinical syndrome of high plasma magnesium (hypermagnesemia) accompanied by somnolence or coma.

4. This may be induced in patients with renal insufficiency by the oral administration of one or more purgative doses of Epsom salt.

5. Many cases of coma in nephritic patients, diagnosed uremic coma, may be simply magnesium coma induced by Epsom salt purgation. Patients could probably be awakened from such coma by intravenous calcium chloride.

6. Sodium sulphate is preferable to Epsom salt for patients with renal insufficiency.

7. There is a clinical syndrome of low plasma magnesium (hypomagnesemia) accompanied by muscular twitching or by convulsions.

8. When this occurs in patients with renal insufficiency, the twitchings or convulsions are relieved by the oral administration of Epsom salt.

**Therapeutics.**—C. DeAsis (Am J Trop Med 14: 33 (Jan) 1934) points out that the clinical manifestations resulting from the bite of *Latrodectus hasseltii*, or the red-back spider, are elevated blood-pressure, slow, often weak, pulse; rapid, often labored, respiration; profuse perspiration; general weakness

and numbness, muscle pains; and paralysis of the lower limbs. The poison may prove fatal. It seems to have a special predilection for the peripheral nerves and nerve endings. The central nervous system seems to be only slightly affected, if at all. The poison travels by way of the lymph canals and is vasoconstrictor in action. A 25 per cent solution of magnesium sulphate, if administered intravenously, is efficacious in the treatment of the bite of the red-back spider. Magnesium sulphate, administered intravenously, is worthy of trial for the bite of *Latrodectus mactans* (black widow spider), since the symptoms produced by this spider and those produced by the red-back spider are in many respects similar, if not identical. The black widow spider is common in parts of the United States, South America and Hawaii.

The intravenous magnesium sulphate treatment, of 371 *preeclamptic toxemias* and 225 *convulsive toxemias* was used by E. M. Lazard (Am J. Obst. and Gynec 26:647 (Nov ) 1933). The objectives of treatment in the preeclamptic state should be (1) to overcome the effects of the toxemia by sedation and elimination, (2) to remove as much work as possible from the embarrassed excretories by proper regulation of the diet, with particular reference to balancing the fluid intake with the output, and (3) to terminate the pregnancy as conservatively as possible, before the onset of convulsions when there is no proper response to treatment. The chief objective of treatment of the eclamptic patient should be the control of the convulsions and the protection of the patient against accidents during the convulsions and coma, surgical termination of the pregnancy during the eclamptic attack is justified only in patients in labor who present some urgent obstetric indication. The necessary sedation and elimination is best secured by intravenous magnesium sulphate in sufficient dosage, aided by intravenous injections of dextrose. The gross mortality in this entire series, preeclamptic and eclamptic patients, was 5.9 per cent. The gross mortality for the active eclamptic patients, was 13.33 per cent, and the corrected mortality 9.5 per cent.

M. P. Rucker (Virginia M. Monthly 61:384 (Oct ) 1934) had a mortality of the same percentage as Lazard in the treatment of 123 cases of preeclampsia with intravenous magnesium sulphate. He gave 20 c c (5 drams) of a 10 per cent solution. If the *convulsions* recurred, he repeated it once or twice. When the magnesium sulphate failed, he used sodium amytal intravenously. In this treatment, rest cannot be emphasized too strongly. If the patient is in labor, he gives **morphine** and **scopolamine** or **sodium amytal** and **scopolamine**, so as to keep her as comfortable as possible in the first stage. For second stage anesthesia he prefers local infiltration of the perineum with 0.5 per cent **procaine hydrochloride**. To avoid the suppression of urine, he gives **plenty of water**. He believes that it is wise to take from 500 to 600 c c of **blood from a vein** in severe cases. After the convulsions are controlled, the treatment is tapered off with small doses of **sodium bromide** and **chloral hydrate**. For several days the **diet** should consist of **fruit juices**.

**MERCURY.—Poisoning.—Treatment**—The recent increase in the number of cases of poisoning is probably due to financial and domestic troubles associated with depression. Over 23,000 persons committed suicide in this country



in 1932 Newspaper publicity plus the ease of obtaining it have led many to use bichloride of mercury in tablet form. This has stimulated the seeking of an effective antidote against acute mercury poisoning. S. M. Rosenthal (Pub. Health Rep. 48:1543 (Dec. 29) 1933) concluded that of several preparations tested on animals, **sodium formaldehyde sulfoxylate** had given the best results in counteracting mercury poisoning. It saved 9 out of 12 dogs from a fatal oral dose of corrosive mercuric chloride, when administered by mouth and intravenously within  $1\frac{1}{2}$  hours after the poison had been taken. The 9 surviving animals were protected against kidney damage, as shown by the lack of elevation of the blood nonprotein nitrogen. In the dogs that succumbed following this therapy or following intravenous therapy only, no significant renal lesions were demonstrable histologically.

The sulfoxylate was used in 10 human cases of acute poisoning from corrosive mercuric chloride, and recovery occurred without appreciable kidney damage (S. M. Rosenthal: J. A. M. A. 102:1273 (Apr. 21) 1934).

Rosenthal recommends the following course of treatment in the use of sulfoxylate:

**Gastric lavage** is done through a stomach tube with a 5 per cent. solution of **sulfoxylate**, approximately 200 c.c. of this solution being left in the stomach. Immediately following this, 10 Gm ( $2\frac{1}{2}$  drams) dissolved in from 100 to 200 c.c. ( $3\frac{1}{3}$  to  $6\frac{2}{3}$  ounces) of distilled water, is slowly injected intravenously, from 20 to 30 minutes being permitted for the injection. From 4 to 6 hours after the completion of this injection, the intravenous administration of from 5 to 10 Gm. ( $1\frac{1}{4}$  to  $2\frac{1}{2}$  drams) of sulfoxylate may be repeated in severe cases. If it is feasible to test the blood serum against corrosive mercuric chloride, the time that this reaction becomes faintly positive or negative (from 3 to 5 hours) may be taken as an indication of the time to give this second intravenous dose of sulfoxylate. If colitis develops later, **high colonic irrigations** with a 1:1000 solution of sulfoxylate should be employed once or twice daily.

If *vomiting* is severe, the use of **morphine** hypodermically may be helpful. If little of the drug is retained in the stomach, the use of **high colonic irrigations** with a 1:1000 solution is indicated.

Commercial samples of technical sodium formaldehyde sulfoxylate are impure and are not suitable for intravenous injection. A purified product should be used, and the solutions should be freshly prepared.

As it is frequently difficult to estimate definitely the amount of a mercurial which has been orally ingested, the advent of an antidote such as sulfoxylate, which may be administered both orally and intravenously, will be a welcome addition to toxicology.

W. B. Porter and C. E. Simons (Am. J. M. Sc. 188:375 (Sept.) 1934) treated 46 cases of mercury poisoning and had 3 deaths. The outline of the treatment which they used follows:

1. Immediate **gastric lavage** with a saturated solution of **sodium bicarbonate**, temperature  $100^{\circ}$  F ( $37.8^{\circ}$  C.) This is continued until the return fluid is clear. The lavage is repeated every 12 hours for the first 5 days.

2. **Morphine sulphate** is administered immediately after the primary gastric lavage (to relieve discomfort, retching and shock).

3. **Sodium bicarbonate**, 500 c.c. (1 pint) of a 5 per cent **solution**, is given intravenously immediately after the lavage, and 1000 c.c. (1 quart) of **normal saline solution** are administered subcutaneously. As long as vomiting persists, the same amount of each solution is repeated every 12 hours

4. **Sodium bicarbonate**, 5 Gm. ( $1\frac{1}{4}$  dram), is given orally every 3 hours during the day and every 4 hours during the night. The urine is kept alkaline to litmus.

5. The total daily **fluid intake** must be at least 5000 c.c. (5 quarts) for an adult, and this amount must be maintained by oral, subcutaneous or intravenous route, dependent upon the ability of the patient to retain the substances taken orally

6. The daily **diet** is orange juice, 500 c.c. (1 pint), milk, 1000 c.c. (1 quart); and beta lactose, 100 Gm. ( $3\frac{1}{3}$  ounces). One egg daily is added as soon as vomiting is controlled. The feedings should be given every 3 hours. If there is vomiting, 10 per cent **glucose solution** is given intravenously in amounts sufficient to maintain an intake of at least 1000 calories. After the first week adequate nutrition and medication are in some cases interrupted by the development of a severe stomatitis and esophagitis. In 2 of the patients of this series a **gastrostomy** was done. It was the deciding factor in recovery.

7. A **colonic irrigation**, using 5 per cent **sodium bicarbonate solution**, is given daily and is continued until recovery is assured.

This treatment modified or prevented the development of the kidney lesions responsible for renal insufficiency and almost totally eliminated colitis.

The leukocyte count has prognostic significance. The 3 deaths in the series occurred in patients with counts above 35,000. Only 1 patient with a leukocyte count above 30,000 per c.mm. recovered.

**Therapeutics**—S. J. Levin (J. Michigan M. Soc. 33: 563 (Oct.) 1934) used the following routine treatment for *impetigo of the newborn* in 44 consecutive cases. It has been successful in clearing up these cases in 72 hours or less, the average duration being 48 hours after the institution of therapy. All mature lesions were opened once or twice a day and the infant was immersed immediately for from 10 to 15 minutes in a bath of 1:15,000 **corrosive mercuric chloride** and a thorough soap bath was given with a mild castile soap. A dusting powder composed of equal parts of **bismuth subnitrate**, light **zinc-oxide** and **mild mercurous chloride** was applied freely following the bath. New lesions were opened twice a day and the bath was repeated. After the first day only an occasional lesion appeared and only one bath was usually necessary. The bath should be continued for a few days after the last lesion appears. The dusting powder is applied freely during this period to the affected parts. Elsewhere, talcum powder is applied freely 2 or 3 times a day, special attention being paid to all folds and creases of the skin. When external heat is indicated, this is best obtained by a **light tent** rather than excessive clothing.

**METHYLTHIONINE HYDROCHLORIDE.** — (**METHYLENE BLUE**).—*Poisoning*.—C. Clemmesen (Ugesk. f. læger 96:37 (Jan. 11) 1934) cautions against the administration of methylene blue in carbon monoxide asphyxia. In 4 cases of grave gas poisoning, from 40 to 50 c.c. ( $1\frac{1}{3}$  to  $1\frac{2}{3}$  ounces) of a 1 per cent. solution of methylene blue was given. In 3 cases the condition became aggravated immediately after the injection, and in the fourth it continued unchanged for an hour, when it was somewhat aggravated. Two of the patients died as a direct result of the intoxication, the third from another cause.

*Physiological Action*.—J. E. Nadler, H. Green, and A. Rosenbaum (Am. J. M. Sc. 188:15 (July) 1934) observed that methylene blue has 2 actions: (1) The oxidation of hemoglobin to methemoglobin. The amount of methemoglobin found immediately following the injection of the average therapeutic dose is small. (2) The drug, used intravenously, excites the individual, and by its rapid elimination into the stomach and urine produced transitory gastrointestinal and urinary irritation. The most frequent toxic symptoms observed were restlessness, paresthesias, a sense of burning in the mouth and stomach, pain in the chest, and strangury. These manifestations usually subsided in from 24 to 48 hours. Electrocardiographic studies show that methylene blue produces a reduction in the height or even reversal of the T-wave, frequently with lowering of the R-wave. This suggests depression of the ventricular musculature. The amount of methemoglobin found and the subsequent decrease in hemoglobin are not of sufficient magnitude to account for the clinical picture described on the basis of anoxemia. Therefore, the indiscriminate use of methylene blue may produce unpleasant results and be dangerous to the patient.

This concurs with Trantmann, who has shown that methylene blue solutions were of no value in the treatment of animals that had absorbed, by breathing, lethal or near lethal doses of hydrocyanic gas in a short period of time.

*Therapeutics*.—In Vienna, illuminating gas is used frequently as a means of committing suicide. During the past 8 months, experiments have been carried on in the Childs Hospital, in Vienna, dealing with the resuscitation by chemical means of persons overcome by illuminating gas. Before the Gesellschaft der Aerzte, F. Deutsch gave recently an account of these experiments. From a series of animal experiments, and taking account of physicians who recommended methylene blue in cyanide poisoning, Deutsch injected a 10 per cent. **solution of dextrose and methylthionine chloride** in cases of *poisoning from illuminating gas*, and achieved excellent results. The exceedingly rapid return of respiration and color in persons receiving such an injection has been remarkable. The preparation effects a rapid detoxication of the blood, with the result that the preparation is changed into a colorless compound (J. A. M. A. 102:711 (Mar. 3) 1934).

**MORPHINE.** —*Untoward Effects*.—*Treatment*.—E. Shute and M. E. Davis (Surg. Gynec. and Obst. 57:727 (Dec.) 1933) state that in *morphine narcosis in the newborn* the **air passages** should be **cleared by** means of a **tracheal catheter**, if necessary, and **external warmth** should be applied. External stimulation is not only of doubtful value, but often serves only to deepen

the narcosis. Such stimuli may cause the baby to inspire once or twice and then lapse into apnea, from which it is difficult to arouse. A mixture of **carbon dioxide** and **oxygen** gases proved to be the most useful stimulus to respiration. The reaction of morphinized babies to these gases is regarded as a criterion of true narcosis. The administration of 30 per cent carbon dioxide with 70 per cent oxygen was the ideal mixture, especially effective when followed by pure oxygen. They present an account of all the fetal deaths in their series, together with the pathologic observations in which necropsies were done. They feel that no baby in their group was lost as a result of morphine narcosis. Indeed, it has been their experience that morphine is a safe drug to use in labor, especially when adequate means of resuscitation are at hand. Many clinicians have relegated this drug to the background because of the possible development of the unpleasant complication of narcosis, only to make use of far more dangerous drugs of doubtful analgesic value.

**Therapeutics.—Labor.**—F. G. McGuinness (Canad. M. A. J. 30:162 (Feb.) 1934) states that until recent years, his preference had been for the use of repeated doses of **scopolamine**, with one small initial dose of **morphine**, usually  $\frac{1}{6}$  grain (0.01 Gm.), together with gas, or a combination of **chloroform** and **ether** in the late second stage. In the hundreds of cases in which this procedure has been followed, there was great relief to the mother but there was a fear as to the possible condition of the fetus. The depressing effect of morphine on the respiratory center seems to be accentuated in the fetus, and many are born in oligopnea and a few in asphyxia, even though a single small dose has been given several hours previously.

**NEOARSPHENAMINE.—Therapeutics.**—Several hundred infections caused by 11 different species of *intestinal protozoa* of man were treated with 3 intravenous injections of from 0.6 to 0.9 Gm. (10 to 15 grains) of neoarsphenamine at intervals of 5 days by W. L. Chandler (J. Michigan M. Soc. 33:27 (Jan.) 1934). Seventeen cases of *amebic dysentery* were treated also, in all of which the organism was absent after 3 injections of neoarsphenamine. Two of these cases were observed over a period of 10 years, during which time 6 stool examinations in one case and 10 in the other one showed no *Entamoeba dysenteriae* organisms. It is believed that these organisms are more easily eliminated from the digestive tract by the use of intravenous injections of neoarsphenamine than some of the other intestinal protozoa. A maximal dose (0.9 Gm.—15 grains—in the case of men and 0.75 Gm.—12 grains—in women patients) has been used by Chandler in all intestinal protozoal infections for the past 13 years. Following the intravenous injection of 0.6 Gm. (10 grains) of neoarsphenamine, the organisms were absent from the third consecutive stool. Often these were not found in the second stool. In one case, in which 0.3 Gm. (5 grains) was injected, the organisms were absent from the second and third stools following the injection, but were found in stools examined 9 months after the injection. In subsequent treatment 3 injections of 0.6 Gm. (10 grains) were given at intervals of 5 days. No organisms were found in stools examined at intervals for several years. These 17 cases represent data of the initial experimental cases. During the past 14

years he has treated a large number of cases with 3 intravenous injections of from 0.6 to 0.9 Gm. (10 to 15 grains) of neoarsphenamine. Symptoms rapidly disappeared, even in cases of liver abscesses and arthritis.

The value of small doses of neoarsphenamine in the treatment of 3 patients suffering from *acute suppuration of the lungs*, who failed to show improvement and were definitely worse after a reasonable time of treatment with the usual conservative measures, were treated with small doses of neoarsphenamine by H. F. Spector (J. Lab. and Clin. Med. 19.66 (Oct.) 1933). There was a drop in the temperature within 24 hours, and the patients improved steadily to complete recovery. In order to confirm these results, Spector treated 21 additional cases of acute and chronic suppuration of the lungs, in the lungs of which clinical spirochetes were found. The initial dose in an adult was usually 0.15 Gm. ( $2\frac{1}{4}$  grains) and was repeated every 4 days until clinical improvement was marked and the sputum became negative for anaerobic organisms. At times the dose was increased to 0.6 Gm. (10 grains); at other times it was decreased to 0.1 Gm. ( $1\frac{1}{2}$  grains), and at other times to 0.05 Gm. ( $\frac{3}{4}$  grain). The number of injections given to an individual patient varied from 1, in a case of *acute putrid bronchitis*, to 14, in a case of *tuberculosis* complicated by fusospirochetal infection. The total amount of the drug used in each case varied from 0.15 Gm. ( $2\frac{1}{4}$  grains) in the former to 2.7 Gm. (42 grains) in the latter case. The best results were obtained when the treatment was started early. Generally, it was observed that very ill patients responded better to the treatment if smaller doses were used.

C. Re (Minerva med. 1.555 (Apr. 21) 1934) states that the treatment of *typhoid fever* with neoarsphenamine should be tested on a large scale. The febrile period is shortened. This indicates that when a rapid improvement of the general condition is evinced, the probability of complications diminishes proportionately and saves the defensive reserves of the organism. The treatment starts with a dose of 0.15 Gm. ( $2\frac{1}{4}$  grains) of neoarsphenamine or, in robust individuals if thought necessary, 0.3 Gm. (5 grains). The preceding dose is repeated at intervals of from 2 to 3 days, or the successive dose is increased. It is not possible to fix a rule regarding doses, but attention must be given to the tolerance of the individual patients.

B. L. Shellhorn and C. Beckwith (Mil. Surgeon 74.239 (May) 1934) state that blood taken early in their case of *tularemia* treated with neoarsphenamine did not show *Bacterium tularensis*. Six injections of 0.45 Gm. (7 grain) doses were administered. The initial lesions began to improve noticeably within 3 days after the first injection. The right axillary gland ceased draining within 24 hours after the administration of neoarsphenamine, at the second admission. The infection was caused by the bite of a squirrel. Infection with tularemia from the bite of an animal is not unusual.

**NITRATE, PHENYLMERCURIC.—Therapeutics.**—The effect of phenylmercuric nitrate was studied in the treatment of fungus and bacterial infections of the skin by B. Levine (J. A. M. A. 101.2109 (Dec. 30) 1933). He used an ointment containing phenylmercuric nitrate in a concentration of 1:1500 by weight, with the addition of 10 per cent glycerin, in a series of 262

cases of *tinea* and *yeast infections of the skin*. Two hundred and five cases were cured; the remaining 57 cases were definitely improved, but these were not followed to completion of treatment.

Phenylmercuric nitrate proved highly efficacious in the treatment of these cases, producing cures when other standard medicaments had failed.

In the great majority of cases no untoward results have been seen from its continued use. In the occasional cases in which irritant effects occurred, these cleared up readily on withdrawal or on substitution of a less concentrated mixture.

All the phenylmercuric nitrate used in this series of cases was prepared by Dr. Ecker and conforms to his specifications.

Phenylmercuric nitrate is presented as a distinct contribution to the dermatologic armamentarium.

**NITRITES (GLYCERYL NITRITES).**—Glyceryl trinitrate in tablet form, when absorbed from the mouth, is by far the most effective agent for relieving the attacks of *angina pectoris* and for their immediate prevention. Of 122 patients treated by W. Evans and C. Hoyle (Quart J Med 3: 105 (Jan) 1934), 86 per cent obtained great relief, and moderate relief was experienced in 11 per cent. Most patients preferred to take the drug at their own discretion, and this method of administration proved more effective than when it was taken at short intervals. Amyl nitrite proved to be disappointing for the relief of attacks and it can be recommended only for those rare cases in which glyceryl trinitrate fails. No harmful results were encountered, though patients used the drug freely for upward of 2 or 3 years.

**OXYGEN.—Therapeutics.**—Observation of the use of effective concentrations of oxygen in *lobar pneumonia* and *bronchopneumonia* over a period of 14 years justifies the view that (1) the symptoms of oxygen want are frequently relieved thereby; (2) that in some cases the function of the lungs is sustained by the provisions of an increased oxygen supply. Both of these effects increase the opportunity for ultimate recovery of the anoxic patients suffering from acute respiratory disturbances, according to A. L. Barach (New York State J Med 34: 665 (Aug 1) 1934).

The method by which oxygen is administered is of great importance. The use of a well-ventilated **oxygen chamber** or **tent** seems preferable to all other methods. A tent which is inadequately equipped with a mechanism for air motion, reduction of temperature and humidity of the enclosed atmosphere should be abandoned in favor of the **nasal catheter** which, although less desirable than a well-ventilated tent, is to be preferred to one in which the hygienic conditions of atmospheric control cannot be employed with moderate effectiveness.

Recommendations in the literature for a more extensive use of carbon dioxide in concentrations of 5 to 7 per cent in *lobar* or *bronchopneumonia* appear unsupported by the theoretical and clinical evidence now available. This type of therapy should be employed in the conditions in which depressed respiration is present, such as CO poisoning, submersion, etc., in which its value has been fully substantiated.

The effectiveness of oxygen therapy in cases of *congestive heart failure*, and its capacity to accomplish a restoration of compensation, has been demonstrated by Richards and Barach. It has been found especially marked in those patients who are free from an active rheumatic process. Patients with degenerative forms of heart disease characterized by myocardial fibrosis, or patients whose myocardial failure is secondary to coronary arteriosclerosis, have shown great improvement as a result of oxygen treatment for a period of 2 to 4 weeks. Its influence in chronic pulmonary conditions such as *emphysema*, *pulmonary fibrosis*, and the *fibrosis* due to end-stage tuberculosis is similar, with the exception that longer treatment is necessary and recurrence of oxygen treatment more frequently needed.

The use of oxygen in *acute coronary thrombosis* has been further observed by R. L. Barach and A. L. Levy (J. A. M. A. 103:1690 (Dec. 1) 1934) with a confirmation of the view that oxygen treatment may be of great importance in this condition because of its sustaining influence on the cardiac muscle function.

Oxygen has been used in the course of an investigation of the influence of **thyroidectomy** in various forms of heart disease. A preoperative period of oxygen treatment was instituted to obtain the highest degree of compensation possible before operation. Oxygen was administered during the operation. A postoperative period of oxygen treatment was employed to avert the consequences of abrupt anoxemia. The favorable postoperative appearance of the 6 patients so treated suggests the use of a similar procedure in cardiac patients exposed to other operations.

Evidence is presented which indicated that oxygen want plays a critical rôle in the causation of *cardiac dyspnea* and the *dyspnea of chronic pulmonary disease*. The relief of dyspnea and the restoration of compensation in these conditions may be accomplished in selected cases by appropriate oxygen treatment; in these cases an elimination of  $\text{CO}_2$  twice as high as the normal concentration suggests that there is no inherent difficulty in passing  $\text{CO}_2$  through the lungs, even in the congested, edematous, or fibrotic state.

John H. Evans (New York State J. Med. 34:679 (Aug. 1) 1934) advocates the use of 100 per cent. oxygen given by a closed mask. He has administered oxygen in concentrations of 80 to 100 per cent. in a series of over 400 cases of *asphyxia*. Many of them inhaled the oxygen for from several days to as long as 4 weeks with as little interruption in the treatment as possible. In cases of *pneumonia*, he gives 100 per cent. oxygen continuously throughout the course of the disease, regardless of whether cyanosis is present or not. Oxygen in high concentration instead of being a death producer, is often a life saver; instead of being a pulmonary irritant, it is an excellent sedative, instead of producing edema of the lungs, it is beneficial for this condition, either reducing it or abolishing it altogether, instead of causing a pneumonia, it is helpful in warding it off and is the best therapeutic agent available for an already existing pneumonia.

M. Friedrich (J. A. M. A. 103:1692 (Dec. 1) 1934) agrees with Evans in the use of high percentages of oxygen and reports a case where concentration of 80 to 95 per cent. was maintained in tent for a period of 6 days.

Anoxemia of the heart muscle occurs after a sudden occlusion of a sizable coronary branch. General oxygen want results and induces impairment of cardio-respiratory activity. The inhalation of oxygen, in high concentration, increases the oxygen content of the arterial blood and results in improvement in the function of the heart.

On the basis of these facts, oxygen has been given, usually in a concentration of 50 per cent, to a series of patients suffering from the effects of *acute coronary occlusion*. In a considerable number, great symptomatic relief has been afforded. Employment of oxygen therapy may aid in maintaining an adequate circulation until the heart has had an opportunity to recover from its acute functional disturbance. In certain instances, effective use of oxygen may be responsible for the saving of life (A. L. Barach and R. L. Levy *Loc cit.*).

If a tent or chamber is not available, the nasal catheter may be employed as a measure of moderate effectiveness. The oxygen should come from a high-pressure tank and be given through a calibrated gauge at the rate of from 5 to 6 liters a minute. This provides about 38 per cent oxygen if the patient breathes through the nose. By placing the catheter beyond the posterior pharynx, so that the tip rests just above the glottis, Wineland and Waters have found that a flow of from 7 to 8 liters per minute is capable of maintaining a concentration of 50 per cent. The method is undoubtedly of value, but the throat must be sprayed frequently with liquid petrolatum to prevent irritation.

In 376 consecutive oxygen-treated cases from the medical and surgical wards of the Presbyterian Hospital, New York, for the years of 1929 to 1932, the mortality of the entire series was 59.3 per cent. The mortality for the medical cases was 55.3 per cent; for the surgical cases, 69.5 per cent. There were 124 cases of *pneumonia* treated in the medical wards with a mortality of 46.7 per cent. In a previous report of 100 cyanotic *pneumonia* patients, the mortality rate was 45 per cent. The complexity of the factors involved in *pneumonia* mortality are such as to prohibit deriving a conclusion on a statistical basis that oxygen therapy lowers the mortality rate in this disease, although a comparison of the results in other series, and observation of relief of symptoms in individual patients, are suggestive of such an opinion. That respiratory function, in respect to the absorption of oxygen, is sustained by effective oxygen therapy in severely anoxic cases of *pneumonia* seems apparent from the reported clinical and physiological studies of individual patients. Administration through the nasal catheter, although a method with mild effectiveness under certain conditions, may be responsible for the prevention of adequate oxygen therapy, because of its use with severely ill patients. Patients who might be relieved of anoxemia by the use of 50 to 60 per cent oxygen, or even 70 per cent oxygen, for brief periods, in the tent or the chamber, at times progress to the point of collapse under the administration of oxygen through the catheter, and may then be incapable of relief even by the transfer to a higher oxygen environment. The use of the tent or the chamber for many cases now treated by the catheter seems advisable. The careful testing of the actual concentration of oxygen breathed by the patient is essential in the employment of the tent or chamber.



J. L. H. Specken (Nederl. tijdschr. v. geneesk. 78:274 (Jan. 20) 1934), who records an illustrative case, emphasizes the value of subcutaneous injection of oxygen in *pulmonary embolism*. The technic is simple and almost painless; 400 c.c. can easily be injected into the subcutaneous tissue of the abdominal wall. The case reported was that of a woman, aged 39, who 4 days after supravaginal amputation of the uterus for chronic endometritis developed symptoms of embolism. No benefit was derived from the administration of stimulants and pantopon, but rapid recovery followed subcutaneous injection of 400 c.c. of oxygen during 3 consecutive days.

**PARALDEHYDE.**—*Therapeutics.*—Paraldehyde is the safest of all analgesics. A. G. Johnson (New England J. Med. 210:1065 (May 17) 1934) found the intramuscular use beneficial in various maniacal and convulsive cases in which morphine had failed to give relief. He considers 8 c.c. (2 drams) an average dose for an adult weighing about 140 pounds (63.6 kg.). The injection should be given deeply into the gluteus medius to avoid sloughing. In the hope of avoiding the pain of intramuscular injection, the intravenous route has been employed in a few cases. A patient suffering terrific pain from a *coronary thrombosis* was given 5 c.c. ( $1\frac{1}{4}$  drams) of undiluted paraldehyde into the vein at the rate of about 1 c.c. (16 minims) in 3 seconds. The patient lost consciousness in about 10 seconds. Coincident with the onset of anesthesia, there was a slight amount of pharyngeal irritation, accompanied by coughing and a strong smell of paraldehyde on the breath. After a few coughs the patient appeared completely relaxed and slept quietly for about an hour. On awakening, the pain was much less severe and could be controlled adequately with morphine. Intravenous paraldehyde, in doses of from 7 to 10 c.c. ( $1\frac{3}{4}$  to  $2\frac{1}{2}$  drams), has been used to control the restlessness and headache of a *hypertension* patient with evidence of extensive cerebrovascular pathologic symptoms. This patient was violently nauseated by morphine, and was unable to retain the barbituric acid derivatives by mouth or rectum. Quiet sleep was induced on each of 6 successive nights by the intravenous administration of 7 c.c. ( $1\frac{3}{4}$  drams) of paraldehyde. Tolerance to paraldehyde unquestionably develops and habit formation has been reported; but these should not be problems if the drug is used only occasionally to control severe pain or convulsive states requiring rapid anesthesia. Although unpleasant, it requires no sterilizing and has a wide margin of safety, while being almost instantaneous in action when administered parenterally.

**PARATHYROID HORMONE.**—*Therapeutics.*—D. V. Conwell (J. Kansas M. Soc. 34:465 (Dec.) 1933) treated 2 patients having *intermittent claudications* and 2 having *thromboangitis obliterans* with parathyroid extract-Collip. Two of the patients were facing certain amputation. The parathyroid extract was given in amounts of 0.5 c.c. (8 minims) or 10 units subcutaneously every other day for 10 injections. The improvement was relatively rapid and uniform. The attacks of intermittent claudication were controlled, permitting at least a temporary return to normal activity. The circulatory changes in the patients having thromboangitis obliterans were prompt; there was a complete control of the pain that had necessitated morphine; return of warmth; moisture,

diffuse reddish hue on elevation of the foot; loss of tenderness; improved sensation and motion of the toes; disappearance of the ecchymoses and deeper discoloration; and there was a return of the pulse in the dorsalis pedis and the posterior tibial arteries. No untoward reactions were observed. **Calcium gluconate** was given by mouth to 2 patients and not given to the other two, but their responses appeared to be equal. The calcium of the blood plasma dropped slowly in one case.

**PHENOLPHTHALEIN.**—*Untoward Effects.*—B. A. Newman (J. A. M. A. 101:761 (Sept. 2) 1933) observed 19 patients with phenolphthalein eruptions in his clinic during the past year. As far as is known, only 3 other substances, antipyrine, arsphenamine (nearsphenamine) or amidopyrine, are capable of provoking identical eruptions. In reviewing the literature, 17 types of atypical phenolphthalein eruptions and 3 types of visceral involvement were assembled, and attention is called to the fact that this drug is not innocuous. The tendency to recur or persist at a site previously that of an initial lesion, together with its exudative character, substantiates the belief that a capillary toxicosis is the key to the pathogenesis. Phenolphthalein is contained in more than 125 proprietary preparations put up in the form of laxative drugs, chewing gums, confections, fruits and biscuits. It is also used for pink icing on cakes, for coloring of candies, and in pink mouth washes and dentifrices.

**PITUITARY GLAND.**—*Therapeutics.*—Two cases of *diabetes insipidus* of undetermined etiology were studied by F. M. Smith (J. A. M. A. 102:660 (Mar. 3) 1934) to ascertain the relative effects of the usual treatment of subcutaneous injections of solution of pituitary and modified treatment by intranasal insufflation of a powdered posterior lobe preparation.

Intranasal insufflation of the powder in doses of from 40 to 50 mg. ( $\frac{2}{3}$  to  $\frac{3}{4}$  grain) 3 times a day was shown to be as effective in maintaining a normal water balance with attendant alleviation of all symptoms, as from 1.5 to 2 cc. (24 to 32 minims) of double strength solution of pituitary administered subcutaneously. The advantages of the powder treatment are ease of application, absence of intestinal, cardiovascular or other side effects, and, most of all, a reduction in cost to less than one-fifth that of the solution of pituitary.

It is conceded that atony of the musculature of the renal pelvis and ureter, with the resultant sluggish drainage of their structures, plays an important rôle in the development and course of pyelitis. Evidence from the literature establishes the fact that certain systemically administered drugs, such as solution of pituitary, augment the tone and peristalsis of pelvic and ureteral musculature. In 16 cases of *pyelitis*, recorded by W. Darley and W. B. Draper (*Ibid.* 102:677 (Mar. 3) 1934), renal pain of relatively prolonged duration was promptly relieved by pituitary solution. The solution was administered subcutaneously in doses ranging from 3 to 15 minims (0.2 to 1 cc.). The intervals between injections varied from 4 to 18 hours, and they were continued until all signs of acute illness had disappeared. The associated symptoms of fever, nausea, frequency and dysuria were also ameliorated, although in a less spectacular manner.

Wm S. Skipp (Endocrinology 18: 596 (Sept.-Oct.) 1934) treated 11 patients suffering from *pituitary headache* (10 women and 1 man) with posterior pituitary extract by mouth, and subcutaneously, with the disappearance of the headaches. The oral treatment consisted of the posterior lobe extract. Extracts of the anterior lobe apparently were without benefit. Skipp explains the headache by an interglandular syndrome that forces the hypophysis to hyperactivity, thus causing it to hypertrophy. As it is contained in the small skull within the large skull, there is an increase of intracapsular pressure, which produces pressure on the blood-vessels and their nerves and the pituitary capsule, and thus causes pain. The sudden and lasting relief received by these patients is remarkable. There is indication that there is a pronounced hypofunction in many cases in which characteristic pain in the head, called headache, would indicate hypofunction.

**PLASMOCHIN.**—*Therapeutics.*—P. Hayden (U. S. Nav. M. Bull. 32: 19 (Jan ) 1934) gave follow-up treatment to 125 men having histories of recent acute *malaria*. Seventy-two were given quinine alone, 10 grains (0.65 Gm.) daily, except Sunday, for a period of 8 weeks. Of these, 17 men, 23.6 per cent., had acute recurrence of malaria either toward the end of the period of follow-up treatment or shortly after its completion. The remaining 53 men were given follow-up treatment of quinine and plasmochin. This treatment consisted of 10 grains (0.65 Gm.) of quinine daily for 3 weeks and 0.02 Gm. ( $\frac{1}{50}$  grain) of plasmochin daily for 6 consecutive days each week for the first and second weeks of treatment. Of the 53 men, only 3, 5.6 per cent., had relapses. The malarial infections were of various types—tertian, quartan, malignant tertian, and mixed. In view of his experience in this respect at Quantico and of reports from other places on the same subject, Hayden is of the opinion that plasmochin should be regarded as an essential part of the postmalarial follow-up treatment and should be administered in combination with quinine.

**POTASSIUM PERMANGANATE.**—*Poisoning.*—The irritant and caustic properties of potassium permanganate render its use repugnant to would-be suicides, it is too easily detected for purposes of homicide, and its characteristic color and immediate causticity make its accidental ingestion rather improbable unless the victim's sensorium is already clouded, according to V. M. Palmieri (Riforma med. 49: 1161 (Aug. 5) 1933). Palmieri reports the strange case of a man who was brought to the hospital *in extremis* by two of his friends, who stated that he had been taken suddenly ill while drinking in a tavern. The first impression, accordingly, was that he was suffering from acute alcoholic intoxication. He was in a state of unconsciousness, with extreme pallor, lips and oral mucosa swollen, a blackish fluid drooling from his mouth, while he made ineffectual attempts to vomit. The pulse was thready, its rate 125 per minute, and his respiration of Cheyne-Stokes type. On the following morning, when his temperature rose to 39.8° C (103.6° F), with abdominal distention, hippocratic facies and complete coma, it became evident that this was no common alcoholic poisoning. A consultation resulted in a diagnosis of acute appendicitis and peritonitis. Operation was out of the question under such grave conditions, and the patient died 31 hours after admission, without regaining consciousness. An

anonymous note now reached the hospital stating that the death was due to a powder put into his wine by friends. Investigation resulted in the discovery that the poisoning was the result of a practical joke played by his drinking companions upon a man already in an advanced state of alcoholic intoxication. The friends of the victim, knowing that he was using local irrigations of potassium permanganate for a gonococcus infection, had conceived the idea of giving him a treatment *per os* to help along his cure. They had, accordingly, introduced 10 Gm. ( $2\frac{1}{2}$  drams) of the substance into his red wine during his temporary absence from the table. On his return he had drunk the glassful at one gulp. Almost instantly he was seized with contortions, became deathly pale, groaned with agony, tried ineffectually to vomit, and fell forward unconscious upon the table. Autopsy revealed a perforation of the posterior wall of the stomach and the presence of acute peritonitis, with signs of caustic action throughout the entire alimentary canal. There was recovered from the stomach 0.173 Gm ( $2\frac{3}{4}$  grains) of potassium permanganate (calculated from the manganese oxide found there).

**Therapeutics.**—Potassium permanganate has been used as a wet dressing and for irrigating wounds; in genitourinary work it makes the best antiseptic. F. C. Warnshuis and B. Vanderkolk (J. A. M. A. 102:1757 (May 26) 1934) successfully treated a case of *gas gangrene* by infiltration of tissue with permanganate solution in strength of 1:500 in the crepitant areas, producing an encircling block. The wound was irrigated with a continuous drip of 1:1000 solution of permanganate.

**PROCAINE HYDROCHLORIDE.**—**Therapeutics.**—The treatment of *spains* by intraligamentous injection of procaine hydrochloride, as originally described by Leriche, is extended and discussed in a report by Arnulf and P. Frich (Presse méd. 42:597 (Apr. 14) 1934). The technic is simple and involves the usual skin disinfection and the injection into the painful periarticular ligamentous tissue of from 0.5 to 1 per cent. solution of procaine hydrochloride, repeated, if necessary, but not exceeding a total quantity of 25 or 30 c.c. (½ to 1 ounce). The rationale of the procedure lies in the blocking of the sensory nerve endings and thus stopping abnormal excitation, obstructing the reflex and interrupting the vicious cycle, in which the phenomena resulting from vasodilatation continuously renew the excitability of the periarticular sensory elements. In both recent and late traumatism, examples of each of which are cited, the results of injections are more favorable and more rapid, than those of the customary immobilization.

**QUINIDINE.**—**Administration and Dose.**—During the past 2 years, H. Gold, H. L. Otto and H. Satchwell (Am Heart J. 9:219 (Dec.) 1933) have followed the clinical course of 21 patients having paroxysmal auricular fibrillation or flutter. In several of those who received quinidine in varying doses—in some up to 50 grams (3.25 Gm.) daily—the attacks remained uninfluenced; in a few others the attacks appeared to have been diminished in frequency or abolished at one time or another, but the influence of the drug could only occasionally be definitely established. Most of these patients were ambulatory. Depression of auriculoventricular conduction by quinidine does not play an important part in

the therapeutic effects of the drug in auricular flutter and fibrillation. In one case reported, however, depression of auriculoventricular conduction by large doses of quinidine was solely responsible for the almost complete symptomatic relief during a period of more than a year. Another unusual aspect of the action of quinidine in this patient was the fact that the frequency of the paroxysms of fibrillation or flutter were not diminished but were nearly doubled during this period. A fixed daily dose of quinidine produces its full effects very early, so that if toxic effects do not occur in the first few days, it is unlikely that they will result from the direct action of the drug when administered over long periods of time. In one patient a daily dose of 60 grains (4 Gm.) of quinidine sulphate prolonged the auriculoventricular conduction time by 20 per cent. and the intraventricular conduction time by 30 per cent. after the first few days; but the continued use of this dose for 364 days did not increase these effects further. Since quinidine is rapidly excreted and shows slight cumulation, the matter of importance in dosage is the size of the daily dose, rather than the total quantity given over a period of time. Evidence is presented in support of the view that the use of a small "maintenance dose" of quinidine to maintain the normal rhythm established with larger dose exerts no appreciable influence on the persistence of the normal rhythm in the ambulatory patient; and that, in general, more intense quinidine effects are necessary to overcome the influences that precipitate an attack of flutter or fibrillation in the ambulatory patient than to abolish an attack while the patient is at rest.

**RHUS.**—*Therapeutics.*—For the treatment and prevention of *rhus toxicodendron poisoning*, G. H. Gowen (J. Allergy 4: 519 (Sept.) 1933) used the almond oil extract of *rhus toxicodendron* in 8 cases, from 5 to 54 years of age. One injection in the spring will protect susceptible persons for approximately 1 year. Injection of the almond oil extract not only is satisfactory therapeutically, but also affords protection for the remainder of the season and leads to milder attacks during the ensuing year. Two patients were immune for 1 year without treatment after several annual injections. In 2 patients who are exposed annually, immunity has been present for 2 years in one and 5 years in the other. The sites of injections were the deltoid in adults and older children, and the gluteal muscles in young children. The skin was sterilized with **tincture of merthiolate (sodium of ethylmercurithiosalicylate)** and the injection was made deep into the muscle. A large drop of collodion was then placed round the site of injection before the needle was withdrawn. This prevented any egress of rhus toxin and eliminated the possibility of any local dermatitis of the skin around this area. In no cases was less than 1 c.c. (1 injection) of extract used. More than 2 injections were never needed.

**SILVER.**—*Poisoning.*—It is a matter of common knowledge that the continued oral use of silver salts may lead to argyria. Because of the occasional outcome of argyria, the oral administration of silver has been largely discontinued. Attention has been called by an editorial (J. A. M. A. 100: 1604 (May 20) 1933) to the fact that the silver content of some of these newer preparations is

not always evident from their proprietary name. H. K. Beckley (*Ibid.* 102:202 (Jan. 20) 1934) reports 2 additional cases of argyria as the result of the indiscriminate use of **neosilvol** in children of 10 and 7 years of age. L. P. Monson (*Arch. Otolaryng.* 19:582 (May) 1934) reports a case of localized argyria of the nasal mucous membrane. A. J. Potek (*J. A. M. A.* 102:787 (Mar. 10) 1934) adds 3 cases to the record from **argyrol** used intranasally, and instillation into the eye.

Although argyria from oral administration is rare at the present time, H. Blumberg and T. Nelson Carey (*Ibid.* 103:1521 (Nov. 17) 1934) report a case of marked argyremia detected during a spectrographic examination of the blood. He summarizes.

1. The spectrographic demonstration of marked argyremia, or high blood silver, permitted the detection of an unsuspected and obscure case of argyria resulting from the oral administration of silver nitrate for gastrointestinal symptoms.

2. The persistence of the high blood silver for more than 3 months after exposure indicated a heavy deposition of silver in the tissues

3. Abnormally high silver was also detected in the urine, feces, cerebrospinal fluid, skin, dental tartar and probably saliva. The presence of the metal in the urine and feces demonstrated that silver was being partially eliminated from the body.

4. Only faint traces of silver were present in the blood and urine in definitely pigmented cases of argyria 10 years or more after exposure, this showed the eventual departure of appreciable silver from the circulation

5. The spectrographic determination of silver in the blood, skin and other parts of the body is an aid in diagnosing obscure argyria and differentiating it from lead or bismuth intoxication

**Therapeutics.**—Various abortive treatments for *gonorrhoea* have been used, mostly with poor success. J. Janet (*Paris méd.* 1:205 (Mar. 3) 1934) for each treatment prepares a fresh solution of 1 Gm. (15 grains) of mild silver protein (argyrol) in 5 c.c. ( $1\frac{1}{4}$  drams) of cold distilled water, which is dissolved in 15 minutes. With a sterilized urethral syringe, from 2 to 5 c.c. ( $\frac{1}{2}$  to  $1\frac{1}{4}$  drams) of the solution is slowly injected into the urethra. The solution is kept in the urethra for 5 minutes. The patient should not urinate for a number of hours after treatment. Very little fluid should be taken during meals, but the patient may drink in the evening after having urinated and early in the morning after having been at stool. Six injections of the 20 per cent solution of mild silver protein are given to the patient at the rate of 2 a day. In successfully treated cases, no gonococci are observed in the morning secretion by the second day. If any are found, the abortive treatment has no value. After 3 days of treatment, the patient is allowed to rest for 48 hours and then another injection is given. Before pronouncing the patient cured, it is advisable to give him 3 glasses of beer before retiring. If, after 2 days, there is no discharge of gonococci, the patient may be pronounced cured.

**SODIUM ISOAMYLETHYL BARBITURATE (SODIUM AMYTAL).—***Untoward Effects.*—Sensitiveness to this drug, as evidenced by skin eruptions, is pointed out by A. M. Langenback (J. A. M. A. 102:17 (Apr. 28) 1934). In 4 cases the eruptions were distributed chiefly on the face, neck, arms, hands and mucous membranes of the lips and mouth. None of the cases showed any sensitivity to the drug when it was first administered, but developed during a period of from 8 to 14 months after the drug had been taken and then discontinued. The primary use of the drug ranged from 9 months to 2 years. The average 3-grain (0.2 Gm.) dose was never exceeded in 3 cases. This sensitivity differs from that previously noted in that it does not extend to other barbiturates.

**Therapeutics.**—After studying a series of 45 cases, M. S. Lewis (J. Tennessee M. A. 26:392 (Sept.) 1933) states that from  $7\frac{1}{2}$  to 15 grains (0.5 to 1 Gm.) of sodium amytal given intravenously and repeated at necessary intervals will absolutely control the convulsions of *eclampsia*. Sodium isoamylethyl barbiturate permits of intelligent treatment of the patient without recurrence of the convulsions.

E. C. Noble (Canad. M. A. J. 31:38 (July) 1934) reports favorable experience with the intravenous injection of sodium amytal in prolonged *hiccup*. A dose of 7 to 10 grams (0.45 to 0.6 Gm.) is given intravenously, or until the patient becomes unconscious during its administration. On account of its tendency to produce pharyngeal paralysis, the patient must remain constantly under observation.

**SODIUM MORRHUATE.**—In discussing sodium morrhuate, H. B. Biegeleisen (Surg Gynec Obst 57:696 (Nov.) 1933) presents the following.

(1) Sodium morrhuate is an unknown, relatively unstable mixture of sodium salts of the unsaturated fatty acids found in cod-liver oil. (2) Its potency diminishes with age and is not uniform. (3) It is occasionally capable of slough formation. (4) No local anesthetic should be added to the mixture. (5) The advisability of incorporating an antiseptic into the solution is open to question. (6) The irritating effect of sodium morrhuate is due to its soapy characteristics and has been duplicated experimentally by a solution of commercial liquid soap. (7) Sodium oleate, which is one of the fatty acid salts present in sodium morrhuate, has been tested and found to possess sclerotic power. (8) The continued testing of the other fatty acid salts present in the mixture is necessary if a standardized pure product is to be developed.

**Therapeutics.**—E. Floyd and J. L. Pittman (J. M. A. Georgia 23:63 (Feb.) 1934) used a 5 per cent solution of sodium morrhuate in injection treatment of *hydrocele* because of the uniform results that were obtained with its use in the injection of varicose veins. Recently, however, they added to it a 0.5 per cent solution of **phenol**. This was done to make it more bactericidal. After preparation of the skin with **mercurochrome**, a small welt is made with a 1 per cent solution of **procaine hydrochloride** over the most dependent portion of the sac. A large caliber needle is then inserted into the sac and the fluid is withdrawn. In order to alleviate the initial pain, a 2 per cent solution of **procaine hydrochloride** is used as a local anesthetic in the sac itself, only a small amount being

instilled, allowed to remain 3 minutes, and then withdrawn. The solution is then instilled. Ordinarily, 8 c c. (2 drams) of the fluid is used and allowed to remain 1 minute. One-half of this amount is withdrawn. A little manipulation is then done and a snug-fitting support is applied. The patient is sent home and for the next few days there is some swelling of the parts. A week later the scrotum feels firm and may contain some fluid. There is usually only a small amount and this is absorbed in 10 days. The swelling and firmness disappear eventually and the cure is complete within a month. Rarely is palpable induration of the sac present after this period of time. It is felt that the sclerosing solutions will obliterate the sacs of the acquired, uncomplicated hydroceles. It must be understood that this method is applicable only in selected types of hydroceles. The radical removal of the hydrocele, however, is such a simple surgical procedure that the reviewer considers the injection treatment questionable.

W. M. Cooper (Am. J. Surg. 21:408 (Sept.) 1933) reports his results with sodium morrhuate in the treatment of *varicose veins* in more than 600 patients with about 4000 injections. The only untoward reaction noted in his early use of 5 per cent. sodium morrhuate was an occasional mild to moderate dermatitis with annoying pruritus. The patients presenting this complication had been treated with large quantities (10 c c.—2½ drams) of the solution. Since limiting the quantity injected at 1 visit to 5 c c. (1¼ drams), Cooper has rarely seen this complication occur. Occasionally, an injection of sodium morrhuate in 5 per cent. strength is followed by a rather widespread reaction in and around the vein, characterized by infiltration, thickening, tenderness and reddish discoloration. This reaction may extend for a distance of 18 to 20 inches along the course of the vein, suggesting a rather widespread phlebitis and periphlebitis, but the patient has no chills or febrile reaction and in a few days the swelling and tenderness begin to subside. Not one case of ulcer or sloughing due to the injection has occurred in his series of cases. A comparison of the results obtained with sodium salicylate, quinine hydrochloride and ethyl carbonate, and with 5 per cent. sodium morrhuate leads Cooper to conclude that sodium morrhuate is more effective, safer and attended with fewer dangers and complications than the other agents.

Sodium morrhuate has been widely accepted as the solution of choice for the obliteration of *varicose veins*. The experiences in general of L. M. Zimmermann (J. A. M. A. 102:1216 (Apr. 14) 1934) have been extremely favorable. In certain cases, however, *sensitization to the solution* may exist or may develop. In 2 reported cases this sensitization manifested itself in a severe general shock-like reaction, while in 2 others, skin manifestation occurred. It is urged that the possibility of such a reaction be kept in mind, just as in all other intravenous injections of possibly allergic substances, and that, particularly in patients who have received morrhuate injections followed by a rest period of several weeks or more, intracutaneous skin tests be made to preclude the danger of a serious anaphylactic response.

**SODIUM PERBORATE.**—*Therapeutics.*—Sodium perborate has been used in the treatment of *Trichomonas vaginalis* in a solution of 10 grams (0.6 Gm.) to the ounce (30 c c.). This freshly prepared solution is injected by means



of a 3-ounce ear syringe into the vagina night and morning, and continued during menstruation. With faithful adherence over 1 or 2 months, the patient may stop all injections and be free of symptoms, according to W. Smith (Wisconsin M. J. 33:101 (Feb.) 1934).

**SULPHUR.—*Therapeutics.***—A. Langeluddeke (Deutsche med. Wchnschr. 60:398 (Mar. 16) 1934) introduced the sulphur treatment of *schizophrenia* in 1927. At first he used a 1 per cent oily suspension of sulphur for the intramuscular injections, but because of pain, this was abandoned and now a 0.5 per cent. sulphur preparation is being used which, in addition to the sulphur, also contains an anesthetic. He begins the injections with 2 c.c. ( $\frac{1}{2}$  dram) and repeats the treatment every second day. At the second and third injections, the same dose often produced a higher temperature; however, in cases in which the temperature had a tendency to decrease with successive injections, the dose was increased by 1 to 2 c.c. ( $\frac{1}{4}$  to  $\frac{1}{2}$  dram). The treatment was considered as completed only after at least 6 injections had been given. The general reactions are comparatively mild and the dangers are much less than in malaria therapy. In order to be able to determine the value of this sulphur therapy, Langeluddeke compared the 35 schizophrenic patients treated with sulphur with 60 who had not been treated. He found that among the treated cases, the number of those who showed improvement was more than 20 per cent higher than among those who had not been treated.

**TANNIC ACID.—*Therapeutics.***—The gross similarity of *decubitus* to certain burns, suggested to W. O. Latimer (J. A. M. A. 102:751 (Mar. 10) 1934) the rationale of treating suitable lesions with tannic acid. Bligh treated an abrasion with tannic acid and Maddock used it to treat the surface from which Ollier-Theirsch grafts were removed. A fresh 5 per cent. aqueous solution of tannic acid is used. Treatment is begun at the first sign of tissue disturbance, preferably before the skin is broken. The wound and surrounding skin are cleansed, and all crusts, débris, and macerated skin are removed. Lesions that may be kept exposed to the air are sprayed every hour with the tannic acid solution, while between treatments, the region is kept exposed to dry heat from electric lights or an electric hair drier. Wounds that must be dressed to be kept clean or to prevent direct pressure are covered with sterile gauze, which is kept saturated with the tannic acid solution. Treatment is continued until a heavy coagulum is formed, which usually requires from 24 to 48 hours. Afterwards, no dressing is applied nor is sterile gauze used to keep the coagulum clean and dry. Healing occurs as in burns, and as the coagulum separates at the edge, it is clipped away. If, during treatment, an infection occurs under the coagulum, the crust should be removed with sterile petrolatum, and the tannic acid reapplied. Latimer concludes that the results in lesions of varying width and depth have been far more satisfactory than in any other method used for control of lesions. The results have been specially gratifying in lesions following cord injuries, in bedridden diabetic patients, and in lesions under casts.

In a number of large *superficial abrasions*, such as those following motor accidents as well as in *bed sores*, B. Pollack (*Ibid* 102:1322 (Apr. 2) 1934)

has used tannic acid with excellent results. He believes it has greatly facilitated the nursing care, greatly relieved pain, and to a large extent, decreased infections.

A great many errors are made in the use of tannic acid. It should be prepared fresh daily and left in the ward or at home in the form of a powder. Roughly, a tablespoonful to an ordinary atomizer makes an efficacious solution, approximately 10 per cent. This should be sprayed every 15 to 30 minutes and no dressings used. It is best to spray for longer than the usual 24 hours and frequently for days. This is of value, as it helps to keep tanned the cracks and breaks that frequently form, thus lowering the possibility of infection. Another error frequently found at this point is the discontinuance of **heat**. The heat keeps the area dry, lowers the risk of infection, and at the same time promotes healing, obviating any need over a partially healed area of dressings or clothing which in themselves are conducive to infection.

**THALLIUM POISONING.**—W. Ludwig and H. Ganner (Deutsches Arch f. klin. Med. 176:188 (Dec. 12) 1933) describe 3 cases of acute thallium poisoning. The patients at first did not admit having ingested thallium, and the disturbances were not correctly diagnosed until the characteristic loss of hair set in. The initial *symptoms* are paresthesia and severe pain in the extremities, particularly the legs. Intestinal disturbances of a colic-like character may develop within the first 48 hours, but, as a rule, they do not become manifest until several days later. Renal disturbances in the form of albuminuria and cylindruria occur, generally during the first week. The cardiac disorders that present themselves within the first 2 weeks are tachycardia, weak pulse, and, occasionally, stenocardial symptoms. Acute dilatation and collapse may threaten. Insomnia appears early and is much complained of. It may be partly caused by the severe pains, but, as a rule, it persists after the pains have disappeared, consequently the intoxication as such must play a part. Disturbances of the bladder, in the form of inhibition of micturition or of incontinence, exist for a number of weeks and incontinence of the bladder may be accompanied by that of the bowel. The pathognomonic loss of hair generally sets in during the third week following the ingestion of the poison. Changes in the nails (white streaks) and, in one case, cutaneous changes in the nail bed were noted. It is thought that the initial paresthesias and pains in the extremities were a manifestation of polyneuritis, which in 2 cases later developed into a degenerative-atrophic paralysis. Involvement of some of the cerebral nerves (facial and recurrent), although rare in thallium poisoning, has been observed in 2 cases. The functional disturbances of the bladder were probably caused by an impairment of the spinal nerves. Whether the temporary ataxia, which in one patient involved all the extremities and the trunk, was of central or neuritic origin, could not be determined. Metabolic tests revealed abolishment or reduction of the specific dynamic protein action.

**THEELIN.**—*Therapeutics.*—R. M. Lewis (Am. J. Obst. and Gynec. 26: 593 (Oct.) 1933) showed by carefully controlled work that theelin treatment induces marked proliferation of the vaginal mucosa of children, thus effecting an approximation of the adult type. This effect was utilized in the treatment of *gonorrheal vaginitis in children* with very encouraging results. Supporting evi-

dence in favor of such treatment has since been offered by the report of Joseph Brown (J A. M. A. 102:1293 (Apr. 21) 1934). He found that clinical cure was complete and lasting, as confirmed by vaginal smears taken several weeks after the last injection.

*Technic.*—Theelin, 1 ampoule (50 units), is injected intramuscularly daily, into the gluteal or deltoid regions. Vaginal smears are taken every second day. If at the end of 10 days the slides are negative, then 1 ampoule dosage is continued for 1 or 2 more weeks. If at the end of 10 days from the beginning of injections the slides are positive for the Neisserian organisms, the dosage is doubled and 2 ampoules (100 units) are given daily until 5 or 6 consecutive slides have shown no gonococci. The fact that there is a vaginal discharge sometimes present at the end of a course of treatment is of no consequence, for the microscope shows no specific organisms and no pus cells, but an abundance of squamous epithelium and detritus, which condition is merely the reaction of growth hormone. In 10 to 14 days, this reaction discharge will subside and the vagina will be clean. In no instance is any local treatment to the vaginal mucosa used.

The higher potency oil solution seems to offer a distinct advantage in the treatment of children, since it permits administration of comparatively large dosage with fewer injections.

The work of H. B. Whitehouse (Surg Gynec Obst. 58:278 (Feb 20) 1934) indicates that theelin is of very distinct benefit in the treatment of *painful breasts* associated with deficiency of the follicular hormone. He used theelin (aqueous solution) in 1-c c (16 minim) doses daily for 5 days preceding each menstrual period. The duration of treatment varied in individual cases. In the treatment of 20 patients, 17 showed disappearances of both pain and swelling after a few months' treatment.

R. P. Stetson, C. E. Forkner, W. B. Chew and M. L. Rich (J. A. M. A. 102:1122 (Apr. 7) 1934) repeatedly observed the coagulation time of the blood of 7 patients with *hemophilia* during treatment with ovarian substance or estrogenic substance. A large amount of one or another of 8 different preparations was given over periods of from 28 to 81 days. In no instance was the coagulation time of the venous blood found to be depressed as a result of such therapy. Theelin (estrogenic substance) administered subcutaneously to 2 patients for from 3 to 7 days neither stopped bleeding nor reduced the clotting time.

Estrogenic substance was demonstrated consistently in the urines of patients both under ovarian therapy and during control periods. No correlation could be established between the quantity of estrogenic substance excreted in the urine and the fluctuations of the blood coagulation time.

No clinical improvement was noted which could be attributed to ovarian therapy. In 4 of the patients, hemarthroses developed without obvious trauma or infection, late in the course of treatment.

**VACCINE (COWPOX).**—W. P. Dearing and M. J. Rosenau (J. A. M. A. 102:1998 (June 16) 1934) studied the duration of immunity to smallpox, as indicated by the results of vaccination in 557 medical students who had previously been vaccinated, and in 9 who had never been vaccinated but who had had smallpox. Of 337 students vaccinated 10 years or less after previous vaccination, only 1 gave a primary take; 15, or 4.7 per cent., gave accelerated takes, and

321, or 95 per cent., an immediate reaction. Of the 168 students vaccinated from 10 to 19 years previously, only 6, or 4 per cent, gave primary takes; 50, or 29 per cent, gave accelerated takes; and 112, or 67 per cent, immediate reactions. After 20 years, of 52 reactions, 35, or 67 per cent, were immediate; 13, or 25 per cent., were accelerated; and 8 per cent gave primary takes.

It is welcome news that immunity conferred by a single vaccination usually lasts longer than the traditional 7 to 10 years, and that the benefits conferred extend for 20 years or more in most individuals. Revaccination reinforces protection, and, as the records presented show, is usually a mild experience. Certainly nothing in these facts should alter the procedure of always vaccinating when exposed or when in danger of exposure to smallpox.

The situation with reference to smallpox is interesting. Vaccination of 9 individuals with a history of smallpox who had never been vaccinated gave 4 primary takes, 4 accelerated takes and only 1 immediate reaction. Experience teaches that smallpox usually protects against itself; second attacks are rare. It does not, however, protect so well against cowpox, as the writers' data show. On the other hand, experience in every epidemic of smallpox in which vaccinated individuals were exposed has demonstrated the powerful specific protection afforded by vaccination.

H. H. Donnelly and M. M. Nicholson (*Ibid* 103:1269 (Oct. 27) 1934), from a study of vaccination in 500 newborn infants, conclude that:

- 1 Smallpox vaccination of newborn infants is a safe procedure with negligible complications, with insignificant influence on growth and nutrition, and almost always without fever.

- 2 The skin reaction tends to be smaller and slighter in extent and leaves behind small, superficial scars when Leake's method is used.

- 3 Adjustment between potency of virus and inoculation technique may insure at least 90 per cent. of successful results on first vaccination.

- 4 Since Jenner's time, vaccination of newborn infants has been practiced successfully.

- 5 Newborn infants are highly resistant to successful results, possibly because of the resistance of growing, young tissues, but other factors mentioned may have an effect, as well as still others at present unknown.

- 6 Observations on foundlings in St. Petersburg (Russia), vaccinated shortly after birth and continued until they were 25 years of age, revealed among many thousands of individuals a slight morbidity in the presence of 17 epidemics of smallpox during the 40 years 1826 to 1866.

- 7 Vaccination at birth is a practicable means of increasing protection against smallpox in a large group of society where it is most needed and who are prone to do without this protection for themselves and their community until forced to obtain it at school age.

**VIOSTEROL.** — *Administration and Dose.* — Symptoms of viosterol overdosage in human subjects are reported by C. I. Reed (*J. A. M. A.* 102:1745 (May 26) 1934). The toxicity of overdosage of ergosterol in children and experi-

mental animals has been observed, but there are no extensive or detailed accounts of this condition, except those of Crimm.

Viosterol is a very potent substance; but, at the same time, when properly used, it is a very valuable therapeutic aid.

Even though viosterol toxicity and hypercalcemia often occur together, these conditions are not interdependent but merely concurrent.

Toxicity in man may be recognized very early, even by the subjects themselves, before any serious damage has occurred, and indicates the discontinuance of viosterol. Later, lower dosage may again be administered with good therapeutic result. Such subjects apparently acquire a certain tolerance after a rest period.

Reed administered very large doses of viosterol to more than 300 human subjects for various purposes. Some could tolerate doses of 2,700,000 international units daily for 5 days, while a few developed gastrointestinal disturbances after the administration of 120,000 units daily for 3 days. However, some of these were found to be allergic to the corn protein.

Increased frequency of urination is the most common initial symptom of viosterol overdosage. This is often accompanied by anorexia and persistent nausea, and soon followed by other gastrointestinal symptoms, such as vomiting and diarrhea, and later, loss of weight. The latter is probably accompanied by an increased metabolic rate, which, in turn, is associated with an increase in the urinary excretion of nitrogen. It also appears that the thyroid mechanism is affected by excessive viosterol dosage.

Other and less constant symptoms that have been noted are muscular weakness, lassitude, dull aching in the muscle, dizziness, disturbed muscular coordination and disturbed equilibrium.

Although there has been a widespread impression that viosterol exerts an aphrodisiac effect, this has not been borne out by the studies of Reed, except as the administration of viosterol improved the general health of the subject. The menstrual cycle is affected to a certain extent. In some instances there seems to be a slight tendency to a lowering of both the systolic and diastolic blood pressures. Furthermore, there has never yet been given to any human subject enough viosterol to produce either fibrosis or calcification of the media within the period of time reported.

It appears then that, according to Reed's studies, there need be little apprehension about the administration of viosterol up to 150,000 international units daily for indefinite periods, but larger amounts had better be limited to periods of a few months at the most.

In this series of 300 cases, 43 patients showed *symptoms of toxicity* in varying degrees.

*Onychia* due to chronic hypovitaminosis is reported by Cleveland White (*Ibid.* 102:2178 (June 30) 1934). Seven cases of nail deformities which the writer has observed within the past 2 years, he believes were due to chronic hypovitaminosis, especially B and D. The earliest manifestations were irregular, longitudinal ridges, with short, transverse, semipunctate depressions, and occurred

in individuals who were markedly restricting their diet, either because of obesity, or in order to control the symptoms of another disease.

All the patients were between 35 and 50 years of age and had abstained from butter and all "fattening" foods. There were no subjective symptoms and all nails were involved. Although 2 cases showed subnormal basal metabolic rates, the administration of thyroid had no effect. Psoriasis and ringworm infection of the nails were ruled out.

Various *dermatologic syndromes* and *tongue changes* have been reported to be due to vitamin B deficiency. It is interesting to note that no animal experimental work confirms these clinical impressions. The patients would not permit the removal of nails for histological study.

The *treatment* consisted of large doses of **haliver oil** with **viosterol** and **foods containing vitamins B and G**. The nails of 6 patients became essentially normal and the seventh patient was vastly improved.

**ZINC STEARATE.—Poisoning.**—Despite all the warnings, zinc stearate still causes poisoning by aspiration. In 1925, a committee of the American Medical Association received reports of 1313 cases of poisoning, 28 of which terminated fatally. They recommended the use of a special container, and also the discouragement of the use of zinc stearate as a dusting powder, as the evidence from a number of pediatricians was against the value of zinc stearate as a dusting powder. H. B. Mettel (J. Indiana M. A. 27:69 (Feb.) 1934) reports a case of poisoning as a result of its being sprinkled over the baby's face.

# PHYSICAL THERAPY

*by*

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**CONSTANT CURRENT.—MYOSITIS, ARTHRITIS AND DISTURBANCES OF PERIPHERAL CIRCULATION.—Histamine by Cataphoresis.**—It is pointed out by D. H. Kling (Arch. Surg. 29: 138 (July) 1934) that histamine is, according to Sollmann, a product of the cleavage of proteins by acids, ferments, or bacteria. It is found in all tissue extracts and is present in large amounts in the normal stool. But it, in turn, is rapidly destroyed by bacteria and is therefore not effective when given by mouth. Subcutaneous or intravenous injections of histamine have powerful effects upon the circulation and smooth muscles. It is partly responsible for the ergot-like effect on the uterus; it constricts bronchioles and the larger arteries and dilates the arterioles and capillaries. Injections of quantities of more than 1 mg. ( $\frac{1}{65}$  grain) may therefore cause alarming symptoms, consisting of headache, vomiting, a fall in blood-pressure and respiratory disturbances.

A simple experiment demonstrates the powerful influence of histamine on the peripheral circulation. One drop of a 1:1000 solution of histamine is placed on the skin, which is subsequently pricked by a sharp needle. Within 5 minutes an urticarial wheal surrounded by a red flare will develop. The response of the peripheral circulation consists of a triple reaction: (1) a local dilatation and an increase in the blood flow in the minute vessels (purple spot); (2) a local increase in the permeability of the capillaries, which produces the wheal; and (3) a widespread dilatation of the surrounding arterioles (flare).

**TECHNIC—Cataphoresis.**—Deutsch devised for the purpose of cataphoresis a battery galvanic apparatus; he used lead impregnated with histamine in conjunction with it. Kling used the following technic:

A galvanic apparatus equipped with an accurate milliammeter supplies the electric energy. For electrodes lead foil is used. Blotting paper is moistened with a 1:1000 aqueous solution of histamine acid phosphate and applied to the affected part. The positive electrode is adjusted over the blotting paper and secured with rubber bandages. Because of the danger of producing burns, care must be taken that the electrode does not touch the bare skin, and all metal should be removed from the vicinity of the current. A convenient negative electrode consists of a nonmetal basin filled with a weak physiologic solution of sodium chloride in which lead foil connected with the negative pole is placed at the bottom of the basin and covered with a rubber sheet. The hand is immersed in the solution. The current is slowly built up to from 4 to 10 ma, about from 1 to 2 ma to the square inch of positive electrode being allowed. The current is permitted to act from one to two minutes.

In the majority of cases not more than a sensation of prickling is felt over the treated part. The current is gradually decreased, contact should not be interrupted suddenly.

**Bettmann Modification**—A nonmetallic (glass, enamel) basin is filled with a 1:10,000 solution of histamine and connected with the positive electrode, it is insulated by a cover of rubber sheeting. The affected extremity is submersed in the histamine. The negative electrode is wrapped in insulating material (linen, towels or rubber) and applied as a cuff over the part to be treated. The current is permitted to act for from 5 to 10 minutes. This method is most convenient in infections of the hands and feet. Drawbacks are the large amounts of fluid necessary and the frequent renewal, as the weak solution deteriorates in from 1 to 3 days.

**Scratch Method**—In cases in which a galvanic apparatus was not at hand Kling uses the following method of application of histamine. The skin is cleansed with gasoline, with a sharp-pointed instrument scratches of about

$\frac{1}{4}$  inch in length are drawn over the affected area in vertical and horizontal lines. The entire area is thus divided into small squares. A piece of gauze is saturated with the 1 : 1000 solution of histamine and rubbed into the scratches.

The results in 730 cases collected from the literature are surveyed by Kling. A definite conclusion as to the value of this method is at present possible only in *myositis*. Of 376 patients, 343 were cured or improved; recurrences were noted in 33 patients.

Thirty-two cases of *myositis* are analyzed by Kling. In these cases 24 of the patients were cured or improved, and 8 remained unimproved. Thorough examination and treatment of all of the affected muscles and their antagonists are decisive for the success of the treatment.

Immediate relief of pain and tenderness after the first treatment was of favorable prognostic significance in this group.

Five patients with *subacromial bursitis* and 2 with *tenosynovitis* were successfully treated.

In 151 cases of *arthritis* reported in the literature, 124 of the patients were improved, in 22 cases the arthritis recurred. In Kling's 24 cases of arthritis, 14 of the patients were improved and 10 unimproved.

**ELECTROSURGERY.—CERVICAL EROSIONS AND ENDO-CERVICITIS.—*Electrocoagulation*.**—A series of 120 patients with damaged cervixes during the late puerperium were treated with electrocoagulation by R. L. Barrett (J. A. M. A 103:1516 (Nov. 17) 1934). He found that electrocoagulation produces a complete cellular necrosis and that the sterilizing effect of the heat extends much farther than the visible coagulation, thus, there is a zone around the coagulated area that is lethal to microorganisms. Electrocoagulation is unaffected by quenching in the mucus of the cervical canal and is not subject to the self-limiting action of charring and carbonization that occurs with the actual cautery. This carbonization prevents uniform penetration and destruction of diseased tissue, and there is a far greater tendency to primary or secondary hemorrhage when the slough separates.

The active electrode used was an ordinary ball coagulating tip, the inactive electrode being a woven mesh strip placed about the patient's thigh.

All the treatments were given under local anesthesia of 2 per cent. **nupercaine** applied topically on cotton pledgets. This has given very satisfactory local anesthesia, although when the coagulation is carried out high in the canal, there may be some complaint of uterine cramps. In the cases requiring coagulation high in the canal, it is advisable that a wide dilatation of the cervix should first be done.

In Barrett's experience the best results were obtained by light rather than deep coagulation, the penetration being, as a rule, from 2 to 5 mm.

The first 7 to 14 days following coagulation there is a free leukorrhea, often blood-tinged. By the fifth or sixth week it has been found that the cervix has shrunk to normal dimensions, lacerations are healed, and all eroded surfaces are completely epithelialized.

In his 120 patients, all have completed at least 3 menstrual periods since the treatment. In no case is there evidence of cervical stenosis. Four patients of the private group have been delivered by the vaginal route without cervical dystocia. Four patients are now pregnant from 2 to 6 months. Two patients in the clinic group were treated by electrocoagulation while in the early weeks of an unrecognized pregnancy. The pregnancy was undisturbed. There are 3 women of the group of 120 who still complain of leukorrhea. Two of these patients suffer from *Trichomonas vaginalis* vaginitis and in the third patient the cause of the leukorrhea has not as yet been determined.

All patients in this series were carefully selected to exclude any pelvic inflammatory disease. It is perhaps due to this careful selection that there was no lighting up of pelvic inflammatory reaction following coagulation. All patients in this series were treated in the office or outpatient department. There are no unhealed cervixes and no gross pathologic changes are evident.

Electrocoagulation, according to Barrett, is superior to cauterization in the treatment of cervical injuries in the late puerperium owing to its uniform penetration and destruction of diseased tissue without carbonization.

**EXERCISE.—CHRONIC ARTHRITIS, PHYSICAL THERAPY**  
**IN.**—In the evaluation of the use of various forms of treatment of rheumatoid or atrophic arthritis R. L. Cecil (J. A. M. A 103.1583 (Nov. 24) 1934) sent a questionnaire to 16 physicians in America interested in this form of arthritis. Of the physical agents used, rest received the highest number of votes, 12 out of 16. Massage and exercises received on the whole enthusiastic support, 8 out of 16. Climate received 5 votes, several voters mentioned that a hot dry climate, such as Arizona or New Mexico is especially good for arthritic patients who are also suffering from sinus infection. It was the general opinion that hydrotherapy was of value chiefly in the relief of symptoms.

Hyperthermia by means of short wave or diathermy elicited very little enthusiasm. One physician remarked that there was no theoretical basis for it, as it would deplete an already ill patient rather than build him up.

The principles back of physical therapy in arthritis are age old. L. T. Swann (J. A. M. A 103.1589 (Nov. 24) 1934) states that they are directed toward improvement in local and general circulation, relaxation, and the development of muscles. Good circulation produces healing, and **heat** in any form, dry, moist or diathermy improves circulation, drawing blood to the part. It is the first physical agent to be thought of in arthritis.

The second physical agent used is **massage**. The massage of swollen joints is not indicated, is apt to produce trouble and should never be done. General massage promotes better general physiologic function and better muscle tone and is very beneficial for those who, being bedridden, are unable to take any form of exercise.

**Exercise** is the third physical agent. Active exercise is the best way to secure muscle massage and heat regulation. In exercising, the use of the joint should always be considered for overuse is detrimental to it. Exercises should be directed toward body correction first, by corrective posture exercises as deep

breathing, abdominal muscle control, rib stretching and use of the diaphragm and trunk. Fatigue should be avoided in all cases of arthritis.

Swain also calls attention to the fact that physical therapy can materially aid in the success of the medical treatment, for faulty posture or poor body mechanics, due to whatever cause—fatigue, carelessness, disease—does handicap the body in its work. A crumpled posture with sagged ribs causes pressure and displacement of the thoracic and abdominal organs. Their capacity to do normal work is inevitably decreased. Secretions and muscular activities are changed or inhibited entirely. Even under ideal conditions of rest, diet and hygiene, this unnecessary hindrance to normal physiologic activity may prevent recovery, resistance may never be developed, and the many unknown factors may never be overcome unless the resistance of health can be secured.

According to Swain, the fundamental physiology of the patient with rheumatoid arthritis is not normal. The heat regulating apparatus is disturbed. The circulation is out of order. The basal metabolic rate is very often subnormal. The blood-pressure is low. The function of the gastrointestinal tract is below par. There is always secondary anemia. Much of this disturbed physiologic functioning may be ascribed to incorrect use of the body and faulty posture, which crowds the abdominal viscera. The correction of posture can best be started by **rest positions in bed**, where every case of arthritis should begin. **Regular positions of hyperextension**, with the pillow under the shoulders, with the hands under the head, will expand the chest, widen the costal angle and raise the diaphragm. This raises all the organs of the abdomen, and the normal pump action of the diaphragm gives better circulation throughout all parts of the abdomen and extremities. A 3 weeks' trial of this position for  $\frac{1}{2}$  hour 3 times a day is adequate to convince one of the truth of this statement.

Another position of circulatory importance is the **face prone position**, which is simply lying face down over a pillow. Combined with this corrective work, physical therapy is of immense importance. This consists of **breathing, abdominal exercise, rib stretching** and the **use of the trunk**. **General massage** also stimulates circulation in the extremities, but care must be exercised about touching joints that are inflamed.

While the patient is in bed, **heat** may be used with great benefit. Local circulation is improved by **packs, bakings, diathermy, infrared radiation** and **sunlamps**.

**PERIPHERAL OBLITERATIVE ARTERIAL DISEASES.—Passive Vascular Exercises.**—The principal objectives in the treatment of obliterative arterial diseases, according to L. G. Hermann and M. R. Reid (Arch. Surg. 29:697 (Nov.) 1934), are the relief of pain and the reestablishment of an adequate collateral circulation in the extremity. The active vascular exercises advocated by Buerger, later modified by Allen, as well as all forms of chemotherapy, physical therapy and surgery, contribute greatly to the patient's comfort. These measures, however, fail to bring about a complete or even an adequate restoration of the circulation in the majority of patients, especially in those suffering from extensive organic disease of the peripheral arteries.

In February, 1933, E. M. Landis and J. H. Gibbon, Jr. (Proc. Soc. Exper. Biol. and Med. 30:593 (Feb.) 1933) published a preliminary note on the effects of alternate suction and pressure on the circulation in the lower extremities of a normal subject. They employed from 100 to 120 mm. of mercury negative pressure for 25 seconds, followed by from 80 to 120 mm. of mercury positive pressure for 5 seconds. The skin temperature was measured to detect changes in the blood flow. Landis later stated that they were gathering some interesting and important data concerning the actual increase in the blood flow as brought about by the method of alternate suction and pressure. Until that time, however, they had confined themselves to the problem of discovering the most efficient method of applying negative and positive pressure, with the plan to use that information later in the treatment of patients. Such fundamental physiologic studies will undoubtedly place this form of treatment on a sound basis.

Hermann and Reid designed an apparatus which they call the *Pavæx Apparatus*. This consists of a control box and a chamber into which the extremity is placed.

The patient is placed on a bed or cot, and the extremity to be treated is inserted through a soft rubber cuff into the treatment chamber. Large windows are so arranged that the color of the foot and leg may be observed at all times. A small amount of soap is rubbed on the inside of the glass windows, the glass polished with a soft, dry cloth, so that moisture will not collect on the glass during the treatment. The foot and leg are then elevated several inches above the level of the heart. The treatment chamber is connected to the control box by means of a thick-walled rubber tube. The two main switches on the control panel are turned on, and the selector switches set for 80 mm. of mercury negative pressure and 20 mm. of mercury positive pressure. The rate of alternation is controlled by the knobs just below the main suction dial and main pressure dial on the control panel.

The apparatus automatically changes the pressure within the treatment chamber from the selected amount of negative pressure to the selected amount of positive pressure at the rate of alternation desired. The average rate of one inch cycle is about 15 seconds.

Since August, 1932, Hermann and Reid have given 3769 treatments by the Pavæx apparatus. Over 3000 of the treatments have been given to the 51 patients with organic obliterative arterial disease, 46 of the patients required treatment for both lower extremities.

It is difficult, at present, according to these authors, to express in mathematical terms the benefits which have been derived from this form of therapy. The multiplicity of signs and symptoms (discoloration of the toes, subjective and objective sensation of cold extremities, aching or burning pains in the feet, easy fatigue of the muscles of the extremities, pain in the feet while at rest or intermittent claudication) which are directly or indirectly the result of organic disease of the peripheral arteries, accounts in part for this difficulty. A careful analysis of the results obtained in the 51 patients reported in this work gave the following data: In all the patients who received intensive treatment for 2 weeks or longer there was a definite increase in the surface temperature of the extremity when observed under controlled conditions of temperature ( $20^{\circ}\text{C}$  to

63° F.) and humidity (50 per cent.). Forty-four of the patients (86.27 per cent.) stated that most of the pain disappeared after about 25 treatments of 20 minutes each, extended over a period of about 2 weeks. Six patients (11.76 per cent.) showed only slight symptomatic relief after more than 2 months of treatment. One patient (1.97 per cent.) stated that the pain was not influenced by 3 months of treatment, and no other cause for the patient's pain could be found. Four patients with moderately severe peripheral arteriosclerosis, who were treated 3 times a week for 11 weeks, stated repeatedly that definite subjective and objective evidence of an increase in the circulation in the extremities remains for about 48 hours after each treatment. Hermann and Reid are not prepared to give any information concerning the permanency of this increase in the circulation, but are, however, of the opinion that this form of treatment should be carried out over a period of many months if a permanent increase in the circulation is to be established.

In April, 1934, G. de Takats (J. A. M. A. 103:1920 (Dec. 22) 1934), at Northwestern University Medical School, started to treat obliterative vascular disease with the **Pavæx apparatus** of Hermann.

Only organic types of vascular disease showing little or no spasm were selected, as suggested by the originators of the method. For estimation of the improvement, the claudication, rest pain, cyanosis and the increase in the oscillographic curve were studied.

Group 1.—*Arteriosclerosis Obliterans*.—The average plan of treatment was, as originally outlined by Reid and Hermann, to administer treatment 3 times a week for  $\frac{1}{2}$  hour. Better results seem to be obtained by daily treatment for an hour. All these patients were ambulatory, most of them dispensary patients, coming from a long distance. Six patients received from 50 to 100 treatments; all these noted subjective improvement. It became obvious that objective improvement could be registered only after 2 weeks of intensive treatment, and that 40 or 50 hours of treatment should possibly be given for a real trial of the method.

Group 2.—*Acute Vascular Occlusions (Thrombosis Embolism)*.—Four patients were treated in this group. They received almost continuous treatment, 1 hour on and 1 hour off, through 48 to 72 hours.

The experience of de Takats with this group was very limited. The general conditions of these patients, their tendency to repeated and multiple emboli, and the fact that none of them were treated the first 6 to 8 hours following the embolism, led to complete failure to avert amputation or death. De Takats stated that it would be unfair, however, to condemn the method in this group of cases, which seems to give the most startling results in the experience of Reid and Hermann.

Group 3.—*Thromboangitis Obliterans*.—Two cases were selected, because they showed very little spasm and no evidence of a recent activation. One man, age 51, received 52 one-hour treatments. There was no subjective or objective improvement. Another man, aged 49, received 25 half-hour treatments with no results.

Group 4—*Endarteritis Obliterans*.—This group, strictly separated from Buerger's disease, is the obliterative healed stage of many different chemical and bacterial injuries that affect the intima. For purposes of discussion the writer grouped the frost bites, the syphilitic, tuberculous arteritides, the scleroses due to lead and arsenic, into this group.

In this group there was a marked improvement in all cases, which is due, de Takats believes, to the fact that (1) this is a younger age group; (2) the interference with circulation is in the small arteries and the larger vessels are free, and (3) with the exception of 1 case, prolonged treatment was given.

#### CLINICAL ESTIMATION OF IMPROVEMENT:

1. *Rest Pain*—All patients afflicted with rest pain, which is particularly excruciating in acute vascular occlusion, were promptly relieved during the application of alternating pressures

2. *Intermittent Claudication*.—This is the complaint which brings most of the chronic obliterative vascular obstructions to the attention of the physician. In the arteriosclerotic group, claudication improved in 4 out of 10 patients. In the group with Buerger's disease, no improvement was noted, while in the group diagnosed as endarteritis obliterans, claudication improved from 1 to 6 blocks, from  $\frac{1}{2}$  to 8 blocks, from 6 blocks to a mile, and from 6 blocks to no cramping at all.

3. *Color Changes*—Cyanosis often is seen to disappear during treatment. This was particularly true in the case of frost bites

4. *Oscillometric Curves*—All patients had an oscillometric examination before and during treatment. From these curves, de Takats learned that a high blood-pressure, and particularly a higher curve on the affected side above the obstruction, gives a good prognosis as to the efficacy of treatment. Unfortunately, however, many of the older patients with arteriosclerosis have a low, plateau form of curve above the knees, or no oscillations at all. In 1 case it was possible to improve this flat oscillometric curve. In general, however, it was impossible to see definite changes in the curves. This is not surprising, as the improvement of circulation is probably in the nonpulsatile element of collateral circulation

5. *Healing of Ulcers*—As stated later, the indolent ulcers due to endarteritic processes heal faster and become painless

6. *Effect on Frank Gangrene*—In the cases that were admitted with frank gangrene, amputation had to be performed, except in the case of the girl with septic endocarditis, in whom amputation was considered useless

*Contraindications to Treatment*—On theoretical grounds, *infection* and *venous thrombosis*, appearing separately or jointly, should constitute a serious warning against the use of the machine. Particularly in the infectious type of *diabetic gangrene with osteomyelitis of the toe*, it would seem unwise to use negative pressure. McKittrick and Root pointed out the frequency of a latent streptococcic septicemia in diabetic gangrene. *Venous thrombosis* in the larger vessels often accompanies arterial obstruction. A recent soft clot may readily be mobilized by this treatment. The differential diagnosis of an arterial embolus,

arterial thrombosis and venous thrombosis is important for those using the machine.

*Difficulties of Treatment:*

1. The apparatus is not noiseless.
2. The rubber-cuff connecting the glass-boot with the extremity under treatment is supposed to be soft and adjustable, not causing any venous constriction. Up to the present, no cuff has been suggested or supplied that would maintain the partial vacuum and not produce constriction of the limb.
3. The glass-boot is so constructed that it will encase the extremity above the knee. Reid and Herrmann pointed out the importance of the external and internal geniculate arteries as collateral channels. But many of these patients have arterial obstruction much higher than mid thigh.

It is emphasized by de Takats that the apparatus requires technical modifications, so that it can be used for a longer period of time, that it be noiseless, and that it may encase larger area of the extremities.

At present the method should be under the control of peripheral vascular clinics with facilities of hospitalization, careful selection of cases, and evaluation of results. The therapy is a valuable adjunct to other useful methods already in use. Late results cannot be predicted. They will be governed mainly by the underlying cause and progressive tendency of the vascular occlusion.

**HIGH-FREQUENCY CURRENTS. — HYPERPYREXIA PRODUCED BY PHYSICAL AGENTS.**—Recently a survey of hyperpyrexia produced by physical agents has been carried out by the Council on Physical Therapy of the American Medical Association (J. A. M. A. 103:1308 (Oct 27) 1934). The object of the survey was to evaluate the efficacy and to determine the dangers connected with the production of fever by physical agents.

Of this group questioned, more physicians made use of diathermy than any other method. Radiothermy produced by either tubes or spark gap, came next. Radiant heat, infrared cabinets, hot-water baths, electric blankets, electric light cabinets, so-called nebulized spray cabinets or steam-baths, electromagnetic induction and air-conditioning came in the order named. It would appear, however, that more patients have been treated by diathermy than any other method.

More patients afflicted with dementia paralytica were treated than any other disease mentioned. Multiple sclerosis came next, and then in order syphilis, chronic arthritis, asthma, tabes, gonorrhea, gonorrheal arthritis and circulatory disturbances of the extremities.

The work that has been done up to this time indicates certain definite clinical possibilities; however, the lack of statistical evidence does not warrant publishing the therapeutic possibilities or indications.

Fifteen of the 34 physicians reported untoward results, while 7 replies on this question were too indefinite to tabulate. Thirteen reported burns, most of them being minor burns and due predominantly to the use of electrodes in the diathermy treatment. Some reported burns on the skin surface caused by local action of the high frequency electric field. A total of 4809 patients were treated



by 34 physicians. Twenty-one physicians reported no deaths, while 13 reported 29 deaths.

One physician reported that out of 7 deaths attributable to the treatment given, he believed quite definitely that 4 were due to the humidity in the infra-red cabinet as a complicating factor. Nearly all the physicians reported that they had no complications. However, several did report heat stroke, circulatory collapse, herpes of the cornea, cerebral hemorrhage, albuminuria, tetany and convulsions.

Physicians reported that a complete examination was always made and that any patients with cardiovascular diseases were not given the treatment.

After a careful study of this survey it appears that any type of machine or apparatus may be used with equal success, provided the person in charge is thoroughly competent and the technician under him is attentive and well-informed as to the facts and dangers involved. The Council believes that the technic and administration of this treatment should be given as much study as a surgeon gives to a specialty or certain branch of surgery

The Council believes that to subject a patient to an artificial fever of from  $105^{\circ}$  to  $106^{\circ}$  F ( $40.5^{\circ}$  to  $41.1^{\circ}$  C.), sustained for 5 hours or more, is to subject him to a fairly strenuous cardiovascular functional test. Patients with normal heart, kidneys and blood-vessels tolerate it well, but patients with myocardial degeneration or with valvular, coronary or other cardiac abnormalities, with impaired renal function from organic disease, with excessively high blood-pressure or arteriosclerosis, or with tuberculosis, diabetes or far-advanced syphilis of the central nervous system (late, rapidly progressing neglected cases or patients who are totally demented) do not tolerate such treatment well and should not be subjected to it.

**Contraindications.**—For the reasons given, advanced age (with a few exceptions, 60 years may be taken as an arbitrary limit), cardiac or renal insufficiency, rheumatic endocarditis, aortic aneurism, advanced arteriosclerosis, pulmonary tuberculosis, diabetes, and late neglected neurosyphilis that has progressed to complete dementia, should be regarded as absolute contraindications.

Every patient should undergo a thorough physical examination and clinical investigation.

The Council on Physical Therapy, after studying this problem, realizes that this preliminary survey is far from complete. However, the survey does show that the treatment of disease by means of hyperpyrexia is now established, but that the best method for administering artificial fever induced by physical agents that can be employed with safety, convenience and comfort to the patient and is subject to complete control by adequately trained physicians is not firmly established. The Council believes that this method should be used only in hospitals, surrounded with the safeguards commonly employed in a major surgical operation and under the direction of skilled physicians. The assisting technician should have ample training and experience, and must be capable of recognizing untoward symptoms and know ways of avoiding dangers.

**HYDROTHERAPY.—HYDROTHERAPY IN FEVER.**—In a complete discussion of the fever regimen at Cook County Hospital, Bernard Fantus (J. A. M. A. 103:484 (Aug. 18) 1934) states that antipyresis is indicated only when the body temperature exceeds 105° F. (40.5° C.) in a fever with a relatively short course, such as pneumonia, or 103° F. (39.4° C.) in a prolonged febrile disease, such as typhoid, because such temperatures are in themselves detrimental to the tissue cells. For the reduction of such excessive temperatures, appropriate hydrotherapy offers the only method of real advantage to the patient. Even if these temperatures are not reached, fever patients should from time to time, say, twice daily, be **bathed with cool water** so as to be refreshed, just as healthy persons refresh themselves by a cool plunge on a hot summer day, and a restless and sleepless patient might be given a **cool pack** to comfort and quiet him. Indeed, the main object of hydrotherapy, even when the temperature is excessive, is not mere reduction of temperature, but improvement in the febrile disturbances of the nervous system and the circulation, the stimulation of respiration and of kidney elimination and, what is most important, the raising of metabolic activity and the increasing of resistance to infection. The latter effects of hydrotherapy may be compared to "opening the drafts so as to permit the fire to burn more briskly."

The essential thing to be remembered in attempting reduction of excessive fever temperature is that it is not merely a matter of simple temperature equalization between a hot body and a cool medium, but a matter of circumventing the heat-regulating mechanism, which tends to maintain the fever temperature by the same means by which normal body temperature is maintained, *i. e.*, by peripheral vasoconstriction and increased metabolic activity. The peripheral vasoconstriction must be antagonized, so as to bring the hot blood from the interior of the body under the influence of the cooling medium, this is generally accomplished by appropriate covering in the "packs" or by vigorous rubbing in the baths. By such means these procedures are made less disagreeable as well as more efficient, not only by exposing the blood to the cooling influence but also by preventing shivering with the excessive heat production. During the procedure the skin must be kept red as constantly as possible, and, at the end of it, left red, warm and moist, *i. e.*, in the best condition for heat elimination. If the skin is permitted to stay pale during the bath and allowed to remain pale and cold at its conclusion, the patient feels miserable and shivers, and presently the temperature may be higher than it was before the bath.

**Choice of Antipyretic Procedure.**—This will depend upon the condition of the skin, of the general circulation, of the kidneys, and of the nervous system.

*When the skin is hot and dry*, reduction of temperature is relatively easy—mere **moistening with tepid water** (85° F—29.4° C.) will give the patient comfort. *When the skin is cold*, the blood must be made to flow into the skin by preliminary use of **heat** (105° F—40.5° C.) with **friction** or, if this fails, by a **mustard pack or bath**, supported by a stimulant to the circulation (**coffee or alcohol**). *Cold should never be applied to a cold skin.*

*The feebler the circulation, the gentler must be the procedure.* One should beware of using heroic hydrotherapy in a collapsed patient, even if the internal temperature is very high.

When *nephritis* is present as a complication, **prolonged tepid** (85° F.—29.4° C.) **baths** should be used, rather than cold procedures.

*When the nervous system is depressed*, the sudden impact of **cold water** and **vigorous rubbing** are invaluable to arouse the patient, to make him breathe better, and to take nourishment more readily. When the patient is *restless* and *sleepless*, a suitable **cold wet pack** is the best sedative that can be prescribed for the fever patient.

Fantus gives the following hydiatric procedures, arranged somewhat in order of increasing severity and antipyretic efficiency, that may be needed to meet these various indications:

- (a) Cold head-compress.
- (b) Antipyretic pack.
- (c) Antipyretic ablution, or "sponging."
- (d) Sheet bath.
- (e) Half-bath.
- (f) Full-bath.

(a) The **cold head-compress** is the single most universal hydiatric procedure in fever. It should, without exception or special order, accompany all antipyretic procedures. This compress is useful by itself to lessen febrile headache and to quiet the delirium of the fever patient. It is a wet towel, well wrung out of ice-water, applied to the head like a turban. To be kept cold, it must not be covered, and it should be changed frequently (as often as it warms up) unless an ice-cap is included, which should be done in all severe cases.

*It is a general principle in all hydrotherapy to keep the head cool and the feet warm.* Hence, whenever there is a tendency for the feet to be cold, a properly protected hot-water bag should be kept near them, as a routine accompaniment of all other procedures.

(b) The most useful form of the **antipyretic pack** is the **trunk compress**. It is mild enough to be used even for children and collapsed patients, and it is of value even in cases presenting very high temperatures in the intervals between the more radical procedures. The cold trunk compress for the child is a Turkish towel, for the adult, a sheet folded so as to extend from the axilla to the hips and all around the body. It is wrung out of water at 60° F (15.6° C), covered with dry flannel (but not waterproof), and changed every 2 hours for temperatures above 104° F (40° C). It is changed every hour for temperatures above 105° F (40.5° C) and removed when the temperature falls below 103° F (39.4° C). In a fever with a long course, the temperature points may be set 1 degree lower. If the trunk compress has not warmed up when changing is due, it should not be changed. If the *skin is cold* to start with, a **mustard pack** should be employed.

The **anterior trunk compress** differs from the foregoing in that the wet cloth covers only the front and the sides to the posterior axillary lines, while the dry flannel covering extends round the patient. It is to be preferred, because it

is less disturbing when the patient is very sick and frequent changing is necessary. When changing is due, the flannel covering is opened and the fresh compress slipped in place.

For children and very sensitive patients the **graduated trunk compress** may be ordered. The first application may be at a neutral temperature ( $90^{\circ}$  F.— $32.2^{\circ}$  C.) to avoid shock and fright; and the temperature of subsequent compresses should be reduced progressively by  $5^{\circ}$  F. each time until the desired result has been secured.

The **cold wet pack** is indicated in conditions of febrile restlessness and sleeplessness.

The **mustard pack** is a modification of the wet pack, consisting of the use of hot ( $105^{\circ}$  F.— $40.5^{\circ}$  C.) water to which mustard (one heaping tablespoon per liter—quart) has been added for wetting the sheet (doubled up for this purpose). A dry blanket surrounds the wet sheet, particularly snug closure being made about the neck to keep the mustard fumes from affecting the patient's eyes. Every 5 minutes the skin is inspected for reaction, which first occurs on the surface on which the patient lies; and within 15 to 30 minutes the application should be removed. This powerful appeal to redden the skin should be used whenever, in antipyretic hydrotherapy, redness cannot be brought to the skin by other means. A suitable ablution should be used as a finishing procedure to free the skin from the adhering mustard particles.

(c) Antipyretic ablution (**sponging**) is the simplest and most commonly employed, but also mildest, measure. It may fail to make an impression on high or stubborn temperatures. It is nevertheless, a useful preliminary to more powerful procedures, serving as a test of the patient's reactive capacity.

**Hot sponging** at  $105^{\circ}$  F. ( $40.5^{\circ}$  C.), of portions of the body at a time, followed by a **warm** ( $100^{\circ}$  F.— $37.8^{\circ}$  C.) **alcohol rub** may give satisfactory results as an initial procedure for very *nervous patients*, especially children. The temperature of the water and of the alcohol may be progressively lowered at subsequent treatments, as judgment and experience indicate.

(d) The **sheet bath** is intermediate in potency between the ablution and the tub bath, for which it serves as a valuable substitute when a suitable tub is not available. It should be resorted to when the "sponge" is inadequate to reduce excessive febrile temperature satisfactorily. With the bed prepared as directed for "ablution," a sheet partly wrung out of water, ranging in temperature from  $80^{\circ}$  F. ( $26.7^{\circ}$  C.) down to  $50^{\circ}$  F. ( $10^{\circ}$  C.) according to indications, is placed underneath the patient and wrapped about him so that no two body surfaces are in opposition without wet sheet between them. Then the sheet is chafed until it warms up, whereupon cold water ( $60^{\circ}$  F.— $15.6^{\circ}$  C.) is dashed on by means of a cup and the sheet is again briskly rubbed and patted until "reaction" takes place, as indicated by warming up of the sheet. Then this process is repeated on another part of the body, and the entire surface (arms and legs excepted) is gone over and over again until the sheet does not warm up as readily as it did, until the patient shivers, or until the temperature has been reduced to  $101^{\circ}$  F. ( $38.3^{\circ}$  C.) The procedure may be finished as discussed under "ablution."

The **ice rub** is the sheet bath modified by using a lump of ice, partly wrapped in cheese-cloth and passed over the surface with one hand while the other strokes and pats the part just treated with the ice for not more than 15 seconds in any one place. It adds severity and efficiency to the sheet rub.

**Cold sprinkling** may often be successfully employed instead of a tub bath, when a tub is not available. In the emergencies of "*heat stroke*," it should be carried out wherever the patient with hyperpyrexia is found and even before he is transported to the hospital, where recurrence of the high temperature may call for its renewed use. The sprinkling should be stopped from time to time, to permit "reaction" to take place, and when this finally does not occur as readily as it did before, or when the temperature has been reduced to 101° F. (38.3° C.), one of the finishing procedures is employed.

(e) The **half-bath** is given in a tub containing water that reaches to the navel when the patient is sitting. While "tubbing" is always more or less troublesome for helpless adult patients, it is so easily carried out for small children that for these it should be the antipyretic procedure of choice, whenever the trunk pack proves inadequate.

Half-baths may be prescribed as follows. Neutral half-bath (at 95° F.—34.9° C.) for 5 minutes with constant friction. Finish by cool affusion (at 75° F.—23.8° C.), followed by gentle drying.

For a more vigorous effect a cool half-bath (at 75° F.—23.8° C.) for 10 minutes with friction might be prescribed. Finish by cold affusion (60° F.—15.6° C.) to neck, back and chest. Dry lightly.

In *febrile collapse*, when the skin is pale and cool and the pulse rapid, the following might be prescribed. **Hot half-bath** (at 105° F.—40.5° C.) for 5 minutes, until skin reddens. Finish with brief **sprinkling** (from sprinkling can) of nape of neck with cool water (at 75° F.—23.8° C.) Rub dry.

Still more powerful a stimulant to the skin is the **mustard bath**: Powdered mustard (1 tablespoon to the gallon) is mixed with a little water to form a thick paste and this is folded in a towel in such a way as to form a bag, which is hung in a hot (105° F.—40.5° C.) warm (100° F.—37.8° C.), or neutral (95° F.—34.9° C.) half-bath for 5 or 10 minutes, until the bath is sufficiently impregnated with the oil of mustard. To protect the patient's nose and eyes a sheet may be thrown over the tub. The patient is bathed until the skin reddens.

(f) The **full-bath** is one that reaches to the bather's chin. It must always be given with friction. Rubbing is the keynote to successful tubbing. Two types may be recognized—the graduated bath and the full cold bath.

The *graduated bath* (*von Ziemssen bath*) is given in a tub one-third full with water at 90° F. (32.2° C.) and accompanied by constant rubbing until the skin reddens. Then bucketfuls of cold water are added, so as not to impinge directly on the patient, until the temperature is lowered to 75° F. (23.8° C.) or even 70° F. (21.1° C.) in the course of half an hour. It may be finished with a cold (60° F.—15.6° C.) affusion to the back of the head.

The *full cold bath* (*Brand bath*), the most powerful hydiatic procedure, has made a special reputation for itself in the prevention and treatment of the "typhoid" state (not only of that which occurs in typhoid). It is much more stimu-

lating than the von Ziemssen bath. It might at first be prescribed as follows: A full bath at 85° F. (29.4° C.) with constant rubbing (abdomen excepted in typhoid) for 5 minutes with cold (60° F.—15.6° C.) affusions to head and back of neck for last 2 minutes followed by light drying

If after such initial baths the temperature continues to rise and is not kept within bounds by these given every 4 to 6 hours, Fantus states that the temperature of the bath water is lowered to 75° F. (23.8° C.) and the duration increased up to 10 minutes, provided the patient reacts adequately. The feebler the patient, the briefer must be the duration of the bath, which makes the stimulating effect greatly overshadow the temperature reducing action.

**MASSAGE, MANIPULATION. — MANIPULATIVE TREATMENT FOR THE GENERAL PRACTITIONER.** — Manipulation is a part of physical therapy, and can be used in conjunction with other physical agents. Several articles and books have recently appeared to present in readable form for the general practitioner those manipulations that are useful in general practice. Treatment by manipulations are chiefly used in 4 classes of cases: (1) reduction of dislocations, (2) forcible breaking down of adhesions, (3) soft tissue manipulations, and (4) manipulation of joints in which no actual dislocation has occurred, but where there is a slight defect of a character difficult to describe.

In soft tissue manipulations it must be appreciated that manipulation is something different than massage, although the dividing is not very definite. In the treatment of soft tissue it is necessary to recognize that both fibrositis and local spasm exist. The success of treatment may be gauged objectively by the complete relaxation.

T. Marlin ("Manipulative Treatment for the General Practitioner," Edward Arnold and Co., London, 1934) in the commencement of the treatment uses only a slight pressure, and keeping the pulp of the finger tips in contact with the skin, draws them across the skin at right angles to the direction of the fibers. The muscles are thus subjected to compression against the underlying bony structures, and the offending muscle strand or nodule is subjected to the maximum amount of compression, as if an effort were being made to disperse it with the fingers. This maneuver is repeated, and as the tissues become less sensitive, more pressure is employed.

One or both thumbs may be used. Later it may be possible to use the knuckles. If the movements are slow and steady, the patient can stand practically any pressure, and there is no limit to the amount of treatment up to the time when complete relaxation of the muscles takes place.

Marlin, under soft tissue treatment, gives a manipulation which he calls *inhibitive pressure*. He gives 2 examples. In the treatment of *headaches*, an examination of the neck often discloses tenderness and rigidity in the suboccipital region at the insertion of the upper fibers of the trapezius. Steady traction on the head with the operator's fingers just under the occiput and maintained for a minute at a time will often produce a relaxation of the tender tissues and a relief of the headache. In *hiccough* an inhibitive pressure on the phrenic nerve is a

useful remedy. Stand behind the patient, clasp the fingers around in front of the transverse process of the third, fourth and fifth cervical vertebræ, and press steadily for 1 or 2 minutes with the tips of the fingers.

Marlin gives some useful manipulations to restore free mobility of the scapula in *stiff shoulders*. He calls attention to the fact that attention is apt to be confined to the shoulder joint in the treatment of stiff shoulders, forgetting that in the abduction of the arm beyond a right angle, the scapula must be free to glide over the chest wall. He gives 5 methods of freeing the left scapula:

(1) Stand in front and towards the left of the seated patient, grasp the scapula by insinuating your right fingers under the vertebral border of the left scapula and push with your left hand against the front of the patient's shoulder. Maintain steady traction as long as possible and until the tissues begin to relax. (2) Same as (1), except employ both hands for the pull on the scapula while pushing with your body against the shoulder of the patient. (3) Patient lying on the unaffected side and proceed as in the first method. (4) Patient lying on a treatment table on his face without a pillow, head turned to the affected side, and arms hanging down over the edge of the couch. Operator stands on the sound side and pushes the scapula with both hands away from the midline. (5) Patient seated, operator stands behind him. Pass your right arm in front of him and grasp his left arm above the elbow. Pull his left arm across his chest, and push the left scapula away from the midline with the heel of your left hand.

In joint manipulations the tissues must be relaxed before this measure is attempted, and it usually is advisable to apply radiant heat to the part for 30 minutes previous to the manipulation. Marlin emphasizes that in joint manipulations, after the joint has been carried to the extreme limit of movement by the operator, an attempt should be made to carry it just a shade further, and the hands making the thrust will probably only travel through a fraction of an inch.

In view of the recent publicity of a Canadian physician treating arthritis by foot manipulation, one of the most interesting chapters in Marlin's book is on *foot and ankle manipulations*. He calls attention to the importance of having mobility of the joints of the foot and ankle, and says that this has not received full appreciation and cannot be too strongly emphasized. Also in *stiff or painful feet* anything interfering with the normal mobility of any of the joints of the foot or ankle may cause an extra compensatory action of the muscles of the back. He quotes a case of *sciatica* that was relieved immediately and has had no return of the pain in 8 years by relief of a fixation between the heads of the fourth and fifth metatarsal bones.

In manipulation of a painful foot Marlin believes the start should be made at the ankle, for if increased movement is produced, the patient begins to use that joint consciously and unconsciously, and the tissues around the joint undergo a continual change in tension and tone and the circulation to and from that region improves. In the ankle joint the trochlear articular surface of superior aspect of the astragalus is narrower behind than in front, and consequently any slip of the tibia would tend to be backwards on the astragalus. A part of the anterior margin of the trochlear surface would be put out of action and in dorsiflexion of the foot would impinge on the anterior lip of the articular surface of the tibia.

Marlin emphasizes that for the ankle and the joints of the foot, an effort must first be made to overcome the resistance of the tendo Achillis. He gives 3 methods of doing this:

(1) Patient lying on his back; feet over the edge of the table. Apply traction with one hand behind the heel and the other over the dorsum of the foot. Under this traction, fully dorsiflex and plantar flex the foot several times. Also the heel should be made to go back, down and in while exaggerating dorsiflexion and maintaining traction on the foot, as the outer border of the trochlear surface of the astragalus curves backwards and inwards. (2) Patient lying on his back on a treatment table, the operator stands on the right of the patient for the right foot, lifts the patient's right leg under his left arm, placing the back of the arm against the back of the patient's thigh just above the knee. The left hand grasps the os calcis between the thumb and fingers. Grasp the dorsum of the foot with the right hand and push the foot away from the leg by using both hands. Force can be increased by stiffening the left wrist, flexing the patient's knee and thigh and leaning back against the leg with the left arm, while the right hand continues pushing on the foot. (3) A leather strap 1 inch wide, 5 feet long, with a buckle and punched holes, is passed around the thigh and over the sole of the foot. The knee is extended and the tendo Achillis is stretched.

Some of Marlin's methods for *foot manipulations* are the following:

(1) Patient lying on his back on a treatment table, the operator stands to the left of the patient's right foot, and grasps the back of the heel with his left hand, the front of the forearm lying along the outer border of the patient's foot. The operator's right hand is against the inner border of the lower end of the tibia which he pushes while his left hand puts the whole foot into forced inversion. This opens the astragalo-calcaneal joint. (2) To mobilize the tarsus, the operator stands on the right of the patient, grasps the right foot just in front of the ankle with the left hand and, with the right hand grasping the foot, puts it through plantar flexion, dorsiflexion and inversion. (3) With the operator in the same position, but the patient with his knee flexed and a small wedge like a sand-bag under the tarsal bones, the patient's foot is forcibly flexed over this wedge. This opens up the tarsal and tarso-metatarsal joints. (4) The joints between the bases of the fourth and fifth metatarsals and the cuboid can be opened up by the operator grasping the patient's foot with his left hand so that the left thumb pushing upwards fixes the cuboid, and with his right hand grasping the foot so the finger pressure comes over the fourth and fifth metatarsals. The operator's right hand twists the foot into inversion. (5) The metatarso-phalangeal and interphalangeal joints are manipulated by the operator cupping the palm of one hand over the dorsum of the toes and placing the thumb of the other hand in position on the sole of the foot just proximal to the heads of the metatarsals. Then the toes are carried over the heads of the metatarsals into flexion as far as they will go, and a slight exaggeration of the force exerted by both hands will produce a separation of the joint surface.

**SPINAL MANIPULATION.**—In the methods commonly used for manipulating the spine, whether it be by the "osteopath's twist" or by the forcible movements under an anesthetic as practised by orthopedic surgeons, Thomas Marlin (*Lancet* 2:477 (Sept. 1) 1934) believes that an unnecessary amount of force is used. Hence a movement is desirable which can be done with the minimum amount of force. It occurred to him that, taking a lesson from what he had found in his fingers, he might try to exploit the principle of traction; but the difficulty was to be able to fix the spine at any given level.

Nothing appeared to fulfill the purpose until the idea suggested itself that the end might be achieved if two operators took part in the manipulation. Each operator must be capable of doing either part of the manipulation, and each should know exactly what the other is expecting to do or feel.



A strong couch is required, suitably padded, and with detachable pillow, so that the patient may lie quite flat. It is essential to have the covering of the couch of some material other than leather, and for this purpose a corduroy cloth is recommended. For a physician of average stature, a convenient height for the couch will be about 2 feet.

The patient lies on his face, head turned to either side, and grasps the two top corners or legs of the couch, while the operator at the foot of the couch takes hold of the ankles. An assistant bends over the patient with his hands on either side of the spine, and exerts a considerable pressure vertically downwards on the patient's back at any desired level. The first operator, raising the patient's feet, legs, and part of his body off the couch, gives a steady pull, and, if necessary, augments this with a tug. The assistant may nod or use some prearranged signal to show that he is making his pressure, and the operator at the feet, who meanwhile has been awaiting the signal, pulls at exactly the correct instant. If the assistant's pressure is made at the level of the fifth dorsal vertebra, then the spine from that vertebra upwards will be fixed, so that the movement will tend to be at the articulations between the fifth and sixth dorsals. By suitably altering his hands, the movement can be directed to the lumbosacral or any other level as the assistant wishes.

Certain points should be noted. In this method of manipulation no loud snap takes place. Another point is that in most cases only slight traction on the ankles is sufficient.

**PHYSICAL THERAPY IN TRAUMATIC SURGERY.**—The final aim of the treatment of injuries is the restoration of function. The most common mistake in the use of physical therapy in the after-care of injuries has been that the patient is treated once daily at best, and given the impression that some piece of apparatus is going to help him regain function. Neither that machine nor the surgeon can give the patient the best functional results unless the cooperation of the patient is enlisted so that he will carry out definitely prescribed directions and use these physical agents for long periods daily. These agents should be used on definite written prescriptions. Records of progress should be kept. Signs of recovery should be pointed out to the patient, thus arousing in him the necessary interest in his own progress to hold his cooperation. Where improvement is not being made, the patient should not be encouraged in a treatment habit.

J S Coulter (Internat J Med and Surg 47:409 (Oct) 1934) says that every surgeon should have in his possession several appliances giving **radiant heat**. These appliances do not have to be expensive. The best method to use is a home-made 4-lamp baker. Another form of applying heat is the paraffin bath. For the use of this and other forms of heat, mimeographed instructions\* are given to the patients when instructing them to use heat at home. It is known that the use of heat increases the local circulation of the part, and that good local circulation is essential for the repair of injured tissues. Therefore, this heat should be applied for at least half-hour intervals 3 or more times daily.

One of the most valuable methods for the application of heat is the **whirlpool bath**. A home-made whirlpool bath may be constructed. The temperature of the bath is first 100° F. (37.8° C). The whirling of water under pressure and the air intake enables this temperature to be increased to 115° or 120° F (46.1° or 48.9° C). This is most useful as a preparation for subsequent massage and manipulation in *painful, stiff joints* and *amputation stumps*.

\* The mimeographed instructions for the use of heat as well as directions for the construction of a lamp baker, paraffin bath and whirlpool bath may all be obtained from the Council on Physical Therapy of the American Medical Association.

*Massage.*—Every surgeon should know the elementary principles of massage. He should personally administer massage and motion in the early stage of *fracture* treatment, as long as there is danger of displacement of fragments, and careful management of the splints is required. In the later stages of treatment he should direct the technician definitely in the type of massage and motion required.

*Sprains.*—Physicians generally could learn from trainers of athletic teams, many important points in the technic of the treatment of recent injuries. These trainers are paid to keep men in the game and to get them back quickly if they are injured. They are willing to take time to treat minor injuries, and they use proper massage, bandaging and mobilization.

In the treatment of a severely sprained ankle, the ankle is often tightly strapped and the patient sent home with directions to rest and apply some form of heat. Far better results for the relief of pain and the restoration of function could be secured with the use of **massage** and **graduated muscle contractions**.

*Graduated Muscle Contractions.*—Associated with massage, electrical muscle stimulation of the graduated contraction variety is of great use. In an acute injury, the beneficial results of massage and passive movements are secondary to the stimulation of the circulation. In graduated muscle contractions by electrical stimulation the good results are due to the direct stimulation to the muscles causing physiological contractions, with all the natural changes dependent on such contractions and the mechanical effects due to the direct movement of the joint.

In this method the **faradic current** is used. The operator's one hand controls the current, gradually increasing and decreasing it. The active electrode is in the other hand which is placed on the muscle to be stimulated. Thus, the operator can appreciate the degree of the resulting contraction and can regulate the current with the other hand to secure the desired contraction. An apparatus for this purpose has been devised that can be made for about five dollars.

The operator is enabled to appreciate at once from the flickering of the contraction if the muscle is becoming fatigued. In a sprain these graduated contractions are started soon after the injury, commencing by producing very slight contractions, the patient endeavors to keep the part absolutely relaxed. Thus, muscular wasting is prevented, the movement causes deep massage to the joint structures, aiding absorption and preventing adhesions.

**PERIPHERAL NERVE INJURY.**—*Postoperative Treatment.*—Electrical stimulation of a muscle or nerve has no effect upon the regeneration of the axis cylinders of a sutured nerve, but it does help in maintaining the circulation of the muscles supplied by the injured nerve, thus keeping the muscle in better condition to resume function when the nerve has regenerated. It should be remembered that unless electrical muscle stimulation is correctly performed, the normal muscles may be stimulated, which is not desired. A weakened muscle is easily fatigued, so that in the early stages only a few contractions of each muscle are produced each day.

At first, the **galvanic current** is employed and each muscle must be stimulated individually. The strength of current used is the smallest amount which

will cause contraction of the muscle stimulated. **Radiant heat** should be applied to the parts for 20 minutes previous to this stimulation. Interrupted galvanic stimulation of a muscle may be given by a home-made galvanic battery. Directions for making such an apparatus may be obtained from the Council on Physical Therapy, American Medical Association. The slow sinusoidal current furnished by many machines on the market has the advantage that it is less painful to the patient.

From time to time the muscle should be tested with the **faradic current**, and as soon as it begins to respond to this form of stimulus, it is treated first with the galvanic current and then with the faradic current at the same treatment.

Electrical muscle stimulation is always combined with proper **splintage**, **radiant heat**, **massage** and **muscle reëducation**.

**ULTRAVIOLET RADIATION.**—The Council on Physical Therapy of the American Medical Association recently summarized the therapeutic uses of ultraviolet radiation (J. A. M. A. 102:841 (Mar. 17) 1934).

The evidence available in January, 1934, indicates that ultraviolet rays have a prophylactic and curative effect on **rickets**, **infantile tetany** or **spasmophilia**, and **osteomalacia**. Prenatal irradiation of the mother, and also irradiation of the nursing mother, appear to have a definite and specific preventive influence on rickets. Irradiation may also exert a beneficial action on other disorders of calcium metabolism, but the limits of such action, the conditions under which it may best be produced, and the specific action of the rays have not yet been fully explored.

The benefit derived by patients suffering from **tuberculosis of the bones**, **articulations**, **peritoneum**, **intestine**, **larynx** and **lymph nodes**, or from **tuberculous sinuses**, when the entire body is exposed to carefully graded doses of natural sunlight or of radiation emitted by certain artificial sources of ultraviolet rays, cannot be doubted. The beneficial results of such irradiation appear to be partly due to ultraviolet radiation, but it is probable that visible and infrared rays, as well as the conditions of the atmosphere, also play a certain ill-defined part in the therapeutic effect.

As far as **tuberculosis of the bones and articulations** is concerned, the majority of those who have had extended experience with heliotherapy agree that suitable, graded exposure to natural sunlight is most effective and that exposure to artificial sources of radiation is second best. Nevertheless, under conditions that make natural heliotherapy impracticable, artificial heliotherapy has been shown to be of distinct value. Of the different types of artificial generators, employed when sunlight is not available, the majority of authorities express a distinct preference for the type of generator the spectral emission of which is relatively continuous and approximates most closely the solar spectrum. The same appears to be true in **tuberculosis of the larynx** and **lymph nodes**, whereas, in tuberculosis of the peritoneum and intestine a distinct preference has not been evinced.

Local exposure to ultraviolet rays of **circumscribed tuberculous lesions of the urinary bladder** has been shown to yield distinctly favorable results, but

the method requires special applicators which are not generally available and, above all, special skill and experience in the cystoscopic diagnosis and treatment of the bladder lesions. On **sluggish, indolent wounds** that do not heal or that are abnormally slow in healing, local or general irradiation may have a beneficial effect.

The evidence supports the conclusion that while, in some cases, ultraviolet rays may have a slight therapeutic influence in **secondary anemia**, such influence appears to be limited and, at most, irradiation is to be regarded as an adjuvant to established methods.

Among the diseases of the skin, on **lupus vulgaris** alone can ultraviolet rays be said to act specifically. In other dermatoses (scrofuloderma, erythema induratum, eczema psoriasis, pustular folliculitis, indolent ulcers, furunculosis, acne vulgaris, angioma serpiginosum, parapsoriasis, pityriasis rosea) local or general exposure to ultraviolet radiation may have a favorable action, but the improvement that may result cannot be regarded as a specific effect of the rays. In some cutaneous disorders (eczema, psoriasis, lupus erythematosus, herpes simplex, xeroderma pigmentosum, farmer's skin, prematurely senile skin) exposure to such rays may cause an exacerbation, provoke an attack, or produce other injurious effects.

*Oft-repeated exposures* to ultraviolet radiation over long periods, in persons, especially children, who have a low tolerance (idiosyncrasy) to ultraviolet rays, may lead to degenerative changes in the skin, such as atrophy, anomalies in pigmentation keratoses and even cancer

Grossly *excessive exposure* of the entire body may, in certain cases, cause serious illness or even death. Grossly excessive exposure to a local area may, in some cases, lead to permanent, deleterious changes in the skin

The Council on Dental Therapeutics of the American Dental Association has adopted a report concerning the therapeutic use of ultraviolet radiation for the treatment of oral diseases and conditions. This report, the Council on Physical Therapy believes, will be of as much interest to the general practitioner as to the dentist (J. A. M. A 102:129 (Jan 13) 1934)

It may be admitted that ultraviolet light has some bactericidal properties *in vitro*, but no adequate evidence or references to adequate evidence appear in literature to show the germicidal effects and what may be expected of them when used *in vivo*. No amount of seriousness can be attached to the claim that the deposition of calcium is accelerated when ultraviolet rays are applied locally.

In another portion of the report the advertising under discussion concerns the virtues of the use of ultraviolet radiation in connection with postoperative pain following extraction of teeth or other surgical procedures, whether due to dry socket, infective osteitis or traumatism, during local anesthesia. The extract from the advertising matter recorded all these conditions as being readily suppressed with ultraviolet therapy. In the consideration of this point, the Council on Dental Therapeutics writes:

The response of individual patients following the extraction of teeth or any other surgical procedure, whether due to dry socket, infective osteitis or traumatism during local anesthesia, is variable and depends on a number of factors.

Hence, it would require a great deal of detailed descriptive and statistical evidence to permit of a valid conclusion being reached.

How much of the supposed beneficial effect was due to the heat and how much was due to light of short wavelength is difficult to tell.

Patients suffering from trifacial neuralgia are known to have periods of remission. Conservative neurological opinion holds that the only available method for alleviating trifacial neuralgia is by conservative or radical surgery. Since the claim is contrary to the well-accepted findings of competent workers in the field, it should be obvious that more evidence is necessary.

In the concluding paragraph, the Council on Dental Therapeutics recommended that the Council on Physical Therapy be advised that no adequately controlled evidence had been presented in descriptive literature and advertising matter to warrant the use of ultraviolet radiation in the treatment of oral diseases and conditions.

**IN EYE DISEASE.**—General ultraviolet radiation is of value as an adjunct in the treatment of local disease of the eye, especially in the case of chronic inflammatory disease, and in cases of disease in children, according to F. W. Law ("Ultraviolet Therapy in Eye Disease," John Murray, London, 1934). He uses a mercury quartz lamp for the first 9 exposures, and then uses a carbon arc lamp with tungsten cored carbons for another 9 exposures. These exposures are given 3 times a week.

Law believes that, according to his experience, more has been claimed for general ultraviolet radiation than is justified by the results. This form of therapy is of most value in those diseases which are generally accepted as being an expression of the general condition of the patient, such as debility, or due to undernourishment, or lack of fresh air and sunshine. His results of treatment of **interstitial keratitis** were better than those of other observers, and he believes that other forms of keratitis certainly derive some benefit from general exposure.

For local phototherapy, Law uses a mercury vapor lamp as the source of ultraviolet radiation, owing to its small emission of infrared rays. The Duke-Elder radiation lamp was used. In spite of the difficulty of producing an experimental cataract by short waved energy and although he has never seen a cataract which could be even remotely connected with ultraviolet therapy, the author believes that there is not the slightest justification for carelessness in its application.

In general, Law believes that local irradiation is of more value in its own sphere than general. In the treatment of **corneal ulcers**, except Mooren's ulcer, **superficial keratitis**, especially **neuroparalytic** and **phlyctenular**, **recurrent abrasion** and **conjunctivitis**, he confirms the good opinions expressed by other writers. Healing of corneal lesions is expedited by ultraviolet radiation, but its use has no effect upon the density of the subsequent scar. The irradiation of an established nebula has not, in his opinion, the slightest effect upon it. He states that his number of cases of other eye diseases were too small to allow of generalization as to the effects of local phototherapy, but he is encouraged to continue the treatment of cases of **sclerosing keratitis**, **recurrent abrasion**, **episcler-**

**itis** and **tuberculous iritis**. The method is of less value than is commonly supposed in cases of recurrent and relapsing keratitis, and useless in keratitis due to the effects of gas. It does not appear to have any considerable bactericidal action upon the conjunctiva.

Law believes that much that has been written about ultraviolet therapy is merely fantastic, and that much of the remainder is merely enthusiastic, but in local therapy there is available something more than an adjunct to routine ophthalmic treatment; in selected cases it is the treatment of choice; and in many cases results of its use are dramatic.

**RESUSCITATION.—ASPHYXIA.**—Y. Henderson (J. A. M. A. 103·750 (Sept 8), 103·843 (Sept 15) 1934) states that short of death, there are 3 degrees of asphyxia:

*Apneic Asphyxia*—Brief but intense asphyxia, under complete deprivation of oxygen, is exemplified in *drowning*. Its outstanding feature for treatment is *apnea*—cessation of breathing. The vital machine is little damaged. It is merely stopped. It is restarted mainly by means of **artificial respiration**. **Inhalational treatment** is secondary, although it is often of critical value for the saving of life.

*Acarbic Asphyxia*—More prolonged but less intense asphyxia is exemplified in those cases in which sublethal atmospheres of *carbon monoxide* have been breathed for several hours. The patients are often still breathing, although in profound coma, when removed from the poisonous atmosphere. The vital machine has been so deranged by asphyxia that, without treatment, recovery is slow and painful. In such cases artificial respiration is often not needed, as breathing has not stopped. But if further damage is to be prevented and recovery is to be rapid, **inhalational treatment** is essential. Experience has shown that for rapid restoration of normal conditions the effective means, along with **oxygen**, is inhalation of **carbon dioxide** in proper dilution.

*Chronic Asphyxia*—This form of asphyxia is due to a partial deprivation of oxygen. It occurs in *anemia* and in *heart disease* and is characterized by shortness of breath and continual oxygen debt. **Restoration of red corpuscles** and prolonged inhalation of **oxygen** are the logical treatments.

In all forms of asphyxia this much only is clear. Deficiency of oxygen induces a profound disturbance of the state in which carbon dioxide is normally held in the body and in its amount. Henderson calls this state "*acarbua*." It is the state generally called "*acidosis*" and mistakenly regarded as an intoxication by acid. Restoration of the supply of oxygen overcomes this state but slowly. If injury to the tissues has not gone too far, restoration of **carbon dioxide** by **inhalation**, together with adequate **oxygen**, rapidly and completely restores normal conditions in the body.

**Artificial Respiration and Inhalational Apparatus.**—In such states as the complete *apnea* induced by *submersion in water* or by *electric shock*, even seconds are precious. The prompt application of **artificial respiration** is therefore the measure of primary importance and for this purpose the **prone pressure method** introduced by Schafer is the procedure of choice. It should always be

continued until natural breathing returns or rigor mortis sets in. Lives have been lost by physicians interfering with the policeman, fireman or boy scout who was performing artificial respiration.

In using the Schafer method or any other form of artificial respiration on a victim of drowning, the question of removing water from the lungs may be disregarded. If the body has been in fresh water, the water that reaches the lungs is quickly absorbed into the blood. If salt water is involved, the absorption is slower. In either case, however, there is really no way to get water out of the finer tubes and chambers of the lungs by manipulation. Fortunately, there are generally enough spaces in the lungs still free from water to permit sufficient ventilation under artificial respiration to supply that minimum amount of oxygen which is necessary to maintain life.

Artificial respiration is also the measure of primary importance in electric shock, although it is effective only in cases in which respiration, but not the heart has been stopped.

In connection with artificial respiration, Henderson calls attention to 3 recent practical developments. One is the **tilting board** developed by Eve, in England, and by Cornish, in California. This device is in principle a seesaw on which the victim is laid and rocked slowly through an angle of 30° or more from the horizontal each way. Adjustable pegs are placed in holes in the board at the shoulders and feet to keep the body from sliding. When the head is lowered and the feet raised, the weight of the abdominal viscera acts on the diaphragm to induce expiration. When the head is raised, the movement of the viscera and diaphragm feetward induces inspiration. If the body is completely flaccid, the victim should be laid on his face, so that the tongue will fall forward; otherwise, on his back. The device is quite easily constructed by any carpenter and would probably prove useful at bathing places and in accident rooms of hospitals for use in cases of concussion, morphine poisoning and other conditions of hypopnea and apnea.

An apparatus for prolonged artificial respiration by compression of the chest has recently been described by Kerridge.

The other development is of a different type: it is for use by physicians only. It is the device, recently developed by Flagg, to facilitate the introduction of a sound into the trachea for the administration of **intratracheal insufflation**. It consists of an electrically lighted laryngoscope. Because of the flaccidity of the muscles of the mouth and throat in the victims of drowning and in asphyxial newborn babies, the larynx is readily made visible with this device and a tracheal sound is easily introduced. Through this sound a mixture of **oxygen** and **carbon dioxide** may be blown directly into the lungs. The principle involved is essentially that of artificial respiration by intermittent insufflation, as introduced by the late S. J. Meltzer. There can be no doubt that some victims of submersion, of neonatal apnea, and of collapse under surgical operations, particularly in the thorax, who can be resuscitated in no other way, may be saved by this means.

For administering inhalation in all varieties of cases of asphyxia, the **H—H Inhalator** with the recent addition of a **Flagg device**, affords, in general, the best means of stimulating respiration after *submersion*, *electric shock* and *carbon monoxide asphyxia*. Several thousands of these inhalators are now in use with a

very large saving of life. The **Davis Inhalator** also has been approved by the Council on Physical Therapy. The infant resuscitators of the Ohio Chemical and Manufacturing Company and of the Foregger Company have both been found efficient and have recently received the approval of the Council on Physical Therapy.

The **Pulmotor** has been condemned so frequently in reports by committees of high scientific competence that, except for its name, it would long since have passed as it should, into the limbo of things forgotten.

A device for artificial respiration of a quite different order is the **Drinker apparatus** and one of the same type offered by **Emerson**. It has been used successfully in cases of neonatal apnea and atelectasis but appears to offer no considerable advantages over simple inhalation of oxygen and carbon dioxide in the easier cases of asphyxia of the newborn or over the Flagg technic in extreme cases.

All subcutaneous, intravenous or intracardiac medication is harmful rather than beneficial in asphyxia.

**Conflicting Theories of Asphyxia.**—These are ably discussed by Henderson who states that in the development of resuscitation, practice has outrun theory. Resuscitation by means of carbon dioxide is now justified mainly by the incontrovertible fact that in many forms of asphyxia this treatment is highly effective in saving life. But this fact is not greatly reinforced by theory. On the contrary, it has had to meet an extraordinary succession of obstacles in the form of adverse theories.

The theory that offered the greatest opposition was one based on biochemical grounds. This biochemical theory was beautifully clear and complete. It was based on the principles of physical chemistry. According to that theory, asphyxia develops as follows: Combustion in the tissues of the living body is first anaerobic, sugar breaks up into lactic acid. Under normal conditions, part of this lactic acid undergoes combustion, the remainder was supposed to be reconverted into sugar. Under oxygen deficiency, however, some of this lactic acid failed to be either burned or converted back to sugar. This acid then reacted with the alkali bicarbonates of the blood, neutralized them, and thus decreased the carbon dioxide content and alkalinity of the blood. Asphyxia led to acidosis, and acidosis was acid poisoning.

In close accord with the requirements of this theory, it was demonstrated that a low pH, low alkali bicarbonates and a considerable increase of lactic acid in the blood do occur in the terminal stage of asphyxia and of all related conditions. Biochemists, therefore, gave warning that inhalation of carbon dioxide, which is the anhydrous form of carbonic acid, must intensify asphyxial acidosis dangerously, perhaps even fatally.

Henderson's discussions of practical means of resuscitation dealt strictly with facts. No well-rounded alternative theory was—or is even now—available. With this suppression, **inhalation of carbon dioxide** was successfully introduced into the surgical field where it soon proved its usefulness. Its success was complete in the nonmedical field of carbon monoxide asphyxia, where treatment



administered by the rescue crews of the city fire departments and theory offered no obstacle.

It was found in experiments on animals in Henderson's laboratory that so-called asphyxial acidosis differs profoundly from a true acid intoxication. The alkali of the blood is not lost from the body in asphyxia, nor is it permanently neutralized; it is merely rendered occult. Dogs that had been made truly acidotic by intravenous injection of dilute hydrochloric acid were quickly overwhelmed, or even killed by inhalation of carbon dioxide. On the other hand, animals rendered pseudoacidotic, or acarbic, by asphyxia were quickly restored to a normal condition by such inhalation. And at this point a fact was discovered that may afford a beginning for a sound theory of asphyxia. This fact is that inhalation of carbon dioxide, instead of intensifying "acidosis" in an acarbic animal or man, quickly recalls the alkali bicarbonates in the blood to their normal amount. In this respect carbonic acid (*i. e.*, carbon dioxide) differs from such acids as hydrochloric. The latter would kill at, or above a point ( $pH$  7.0) to which the blood of an asphyxiated man, animal or newborn baby may be acidified with carbonic acid with no harm whatever during resuscitation.

This mobilization of alkali under the influence of carbon dioxide in the presence of oxygen is a vital reaction occurring not only in animals, but even in plants, such as the potato. The contrary reaction occurs in men and animals during the development of asphyxia. Under deficiency of oxygen the carbon dioxide in the blood is also diminished, and following this diminution, a considerable part of the blood alkali is somehow neutralized or immobilized. It is highly significant that this sequence occurs not only during the development of asphyxia under carbon monoxide, but equally in the asphyxia of a baby before birth. The former can lose carbon dioxide through the lungs; the latter cannot. The orthodox theory, which fails in respect to these matters, has failed also, it may be noted, in others. It has failed particularly in respect to the value of alkaline therapy in diabetic acidosis, and extensive revision has been needed in respect to the part supposedly played by lactic acid in muscular contraction. So fallible a theory should not be allowed longer to interfere with the saving of human life.



# DIETETICS

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**DIETETICS.—Oxalic Acids in Foods.**—In an editorial (J. A. M. A. 103: 1152 (Oct. 13) 1934) referring to the presence of oxalic acid in foods, the statement is made that “there is considerable unfounded misapprehension concerning the evil effects of oxalic acid in the diet.” E. F. Kohman, of the National Canners’ Association Research Laboratories in Washington, D. C., has compiled a table in which he shows that almost every fruit and vegetable contains oxalic acid (J. Am. Dietet. A. 10: 100 (July) 1934).

PERCENTAGE OF OXALIC ACID REPORTED IN FOODS.

	<i>Per Cent.</i>
Apples . . . . .	0.005
Asparagus .. . . .	0.009
Beets .....	0.03 to 0.04
Beet greens .. . . .	0.62 to 0.75
Brussel sprouts . . . . .	0.002 to 0.004
Carrots .... . . .	0.013
Cauliflower . . . . .	0.006
Celery stalks . . . . .	0.002 to 0.028
Cherries . . . . .	0.008
Cocoa . . . . .	0.45 to 0.49
Coffee (roasted) .. . . .	0.01 to 0.08
Coffee (beverage) . . . . .	0.002
Currants .... . . .	0.03
Dandelion greens . . . . .	0.0
Endives . . . . .	0.003 to 0.01
Figs, dried . . . . .	0.01 to 0.12
Grapes . . . . .	0.008
Kale ... . . . .	0.0
Kohlrabi .. . . .	0.007
Lettuce, head . . . . .	0.003
Melons .. . . .	0.003
Mustard greens . . . . .	0.0
Onions . . . . .	0.005
Oranges .. . . .	0.01
Pears . . . . .	0.02
Pepper (ground) . . . . .	0.32 to 0.46
Pineapple .. . . .	0.01 to 0.03
Pineapple juice . . . . .	0.007 to 0.03
Potatoes . . . . .	0.04
Raspberries . . . . .	0.05
Rhubarb leaves . . . . .	0.3 to 1.11
Rhubarb stems . . . . .	0.25 to 0.29
Sorrel . . . . .	0.27 to 0.36
Spinach . . . . .	0.29 to 0.69
Spinach, New Zealand . . . . .	1.198
Squash, summer . . . . .	0.003
Strawberries, garden . . . . .	0.01 to 0.06
Strawberries, wild . . . . .	0.06
Tea, black . . . . .	0.37 to 1.43
Tea (beverage) . . . . .	0.0044
Tomatoes .. . . .	0.005 to 0.011
Turnip tops . . . . .	0.0

Kohman points out that an individual would be obliged to eat from 2 to 5 pounds of food containing 0.5 per cent. of oxalic acid, in order to secure a toxic dose.

Japanese laboratories (S. Luzuki: J. M. Sc. Japan. 2: 291, 373, 401, 1934) have shown that this acid is a normal product in the animal body, occurring in the blood in a concentration from 3 to 4 mg. per c.c. A diet of protein or fat when taken for a definite length of time had no effect whatever on the level of oxalic acid concentration, but the ingestion of a carbohydrate diet caused a rise in oxalic acid concentration. This apparent relationship between oxalic acid and carbohydrate metabolism is of interest in view of the fact that derangements of carbohydrate combustion are frequently attended by an increased excretion of urinary oxalic acid. It has been demonstrated that insulin effects an increased ability of the organism to burn this organic acid. There is also a question at present about the formation of calcium oxalate from the calcium in the food, which cannot be absorbed. Since it is very important that a definite amount of calcium be taken daily, and the amount is so often deficient in the average American dietary, it is important that this question be clarified, which no doubt will be soon.

H. C. Sherman ("Chemistry of Food and Nutrition," p. 278, 4th Edit., Macmillan Co., New York, 1932) states that "because of lack of knowledge as to the handling of oxalic acid and oxalates in the body, foods reported as containing these cannot be discussed satisfactorily in this connection. Pineapple and spinach are among the foods so reported."

E. F. Kohman (*loc. cit.*) says it is interesting to trace the reason for pineapple being given special attention because of its oxalic acid content. It is said that new arrivals on the Hawaiian Islands, upon consuming large quantities of raw pineapple, suddenly experience a "soreness and burning of the mouth and esophagus, and discomfort in the stomach, and that a plausible explanation seems to be presented by the calcium oxalate crystals in the juice." Raw pineapple contains a proteolytic enzyme which tends to digest protein. Therefore, raw pineapple cannot be used in making gelatin desserts. Since the mucous lining of the mouth and throat are of protein-like material, the irritating effect from eating pineapple seems clearly explained. Canning destroys the property of this proteolytic enzyme.

Kohman says further that, "If one deliberately undertakes to eat an abnormal quantity of a food at one time it is possible to suffer ill effects, whether that food contains oxalic acid or not." Many foods contain physiologically active constituents, and every individual who eats moderately and with common sense in dietary matters may disregard the question of oxalic acid in foods.

**VITAMINS.—Vitamin and Minerals.**—*Vitamin A*.—According to S. Smith (J. Am. Dietet. A. 10: 109 (July) 1934), the "rapid development in the past few years in knowledge of the structure of certain hormones and vitamins is one of the most striking contributions to nutrition and illustrates the newest of trends—the effort to understand what lies behind normal and abnormal metabolic changes." The writer continues to discuss the question as to the capacity of the human body to convert carotin into vitamin A. Experiments point out that man occupies an intermediate position in his capacity to do so. This may probably account for the reluctance of some of the medical profession to place commercial

preparations of carotin on a par with the natural concentrate of vitamin A, haliver oil. The anti-infective properties of vitamin A are still under discussion. In the government report used in this section it will be noted that the word "may" is used when the anti-infective properties of vitamin A are discussed.

W. Cramer, in a letter to the *British Medical Journal* (2: 1141 (Dec. 16) 1933) under the title, "How Do Vitamins Act?" considers that the mucous membranes cannot be freed from an infected condition, once it is acquired, by feeding vitamin A, but does believe that the membrane may be strengthened, thus avoiding infection, and, if once infected, to prevent further infection. Smith (*loc. cit*) believes that this may be the reason why so many have lost faith in the anti-infective properties of vitamin A, because they have failed to recognize this difference.

H H Beard (*J Am. Diet.* 10: 193 (Sept ) 1934) summarizes the "prophylactic effect of the ingestion of 9 White's 'Cod-liver Oil Concentrate Tablets' daily for 1 year on a group of 36 medical students. There was a reduction of about 50 per cent in the incidence of colds and 68 per cent. of those that did occur, were of the mild type. The incidence of influenza was exactly the same in the group taking the tablets as it was in another group of 100 students not taking them. Later, he refers to an epidemic of influenza which occurred during the study. Of 36 students in the study who had taken the codliver oil concentrate tablets 56 per cent suffered an attack of influenza, while 40 per cent did not."

From studies made on the richness of vitamin A in halibut liver oils, J. A. Lovern (*Biochem J.* 27: 1461, 1470, 1933) has found that the older the fish, the larger the storage of vitamin A which is received from the food. Smith says that all of this has an application in human nutrition. From experiments on liver analysis, it has been found that if from infancy the individual has had plenty of vitamin A, a large reserve will be built up in the liver, and that when the individual becomes an adult, it will not be necessary to take a vitamin A concentrate to build up resistance against respiratory infections during the winter months.

It has been reported that mineral oil tends to wash vitamin A out of the system, or else prevents the complete utilization and absorption of same. J I Rowntree (*J Nutrition* 3: 345 (Jan ) 1931), and more recently H. S. Mitchell (*Proc. Soc. Exper. Biol. and Med.* 31: 231 (Nov ) 1933), shows that 10 times more than the usual amount of spinach was required as the only source of vitamin A, to promote growth at a unit rate in rats. Smith believes that more complicated factors are involved than just the dissolving out of vitamin A by mineral oil.

Studies have been made in which they have shown that urinary calculi are associated with a lack of vitamin A and D. Tests show that there must be another factor or factors, such as "stasis resulting from extensive inflammatory reactions, an imbalance in phosphorus metabolism, and infection. Experiments performed by Bliss, Livermore and Prather on rats led them to the conclusion that vitamin A is of greater importance than vitamin D in the prevention of calculi. Vitamin D may, however, be of indirect influence. Of all the animals on diets deficient in one or both of these vitamins, not one developed calculi. The conclusion is therefore reached that there must be some other influence. "Clinically, one can utilize the results of these experiments by feeding patients who have passed or from whom calculi have been removed, foods rich in vitamins A and D, for it has been

shown that a deficiency of these vitamins causes some metabolic upsets or produces back-pressure and stasis that result in stone formation "

*Vitamin B.*—C. O. Prickett (Am. J. Physiol. 107: 459 (Feb.) 1934) studied the effect of vitamin B deficiency as affecting the central and peripheral nervous system. He finds a deficiency produces no characteristic change in the peripheral nervous system, but brings about very definite changes in the central nervous system, consisting first of disseminated foci of hemorrhage or intense congestion, followed by cellular damage, varying in degree with the length of time the animal is left on the experiment. The areas most consistently affected seem to be the centers for the equilibratory control of the muscles and another is concerned with the transmission of gustatory impulses from the tongue. This may suggest the appetite-promoting properties of vitamin B. Prickett believes that these structural changes simply locate the functional disturbances and that the latter are associated with disturbed carbohydrate metabolism, but that proof of the nature of the disturbance must wait until a pure vitamin B has been prepared in sufficient quantity for experimental work. Inflammation of the tongue, called glossitis, with atrophy of the lingual papillae, found in pernicious anemia and other pathological conditions, often clears up after taking vitamin B.

A. M. Hutter and W. S. Middleton (J. A. M. A. 101: 1305 (Oct. 21) 1933) administered large doses with and without liver therapy to pernicious anemia patients suffering from atrophy of the tongue. In some instances, there was a prompt response in alleviation of the tongue symptoms on high vitamin B intake without specific anemia therapy, in others, there was no response until the liver therapy had been instituted in addition to the vitamin B, while in still others there was no response with and without liver therapy, probably due to impaired absorption and assimilation.

*Vitamin (B<sub>2</sub>) G.*—Smith states that diets which are rich in vitamin B will also furnish vitamin G. Illustrations are given to show that pellagra is more than a simple vitamin G deficiency disease. Cures of pellagra-like lesions in rats have been reported when ventriculin, the commercial preparation of desiccated hog stomach, which has proved so effective in pernicious anemia, was administered.

Sherman a few years ago found that some of the symptoms of vitamin G deficiency in rats were those of premature senility. Recently P. L. Day (Am. J. Public Health, 24: 603 (June) 1934) has produced a condition due to vitamin G deficiency called cataract. Human cataract is more commonly found in the old than the young; Sherman, therefore, may be on the right path with the above statement.

Reports show that pellagra seems to be on the decline. The question is raised, "is this in spite of, or because of, the depression? Are the poor getting more adequate diets because they are on relief or are they paying more attention to home gardens? Smith believes that it would make an interesting study to compare the quality of food eaten this year and last year by the pellagrins who have not as yet had a recurrence."

*Vitamin C.*—Vitamin C, ascorbic acid, is an active oxidizing agent, according to Smith (*loc. cit.*), and a chemical method has been developed to determine its distribution. When guinea-pigs were deprived of vitamin C, this vitamin dis-



appeared rapidly from the adrenals. Considerable time elapses between the disappearance of vitamin C from the adrenals and the development of gross symptoms of scurvy. A. E. Siehrs and C. O. Miller (Proc. Soc. Exper. Biol. and Med. 30: 696 (Mar.) 1933), who observed the above, are of the opinion that the symptoms of scurvy are only secondary changes arising as a result of altered metabolism. They say, remembering that man resembles the guinea-pig in the need of a continuous replenishment of vitamin C, it is safe to conclude that there is a similar wide margin between depletion of body reserves of vitamin C deficiency and actual scurvy. Work is now under way to find a means of detecting sub-clinical scurvy in man by determining the capillary resistance.

It is of interest also to note that D. T. Smith and M. McConkey (Arch. Int. Med. 51: 413 (Mar.) 1933) have been able to produce peptic ulcers in guinea-pigs by placing them on diets partially deficient in vitamin C. Smith states that this may possibly occur in man, and suggests that his diet should then contain an abundance of vitamin C, which of course it does not, for the peptic ulcer diet, unfortunately, is often lacking in vitamin C. The same investigators also found that a plentiful supply of vitamin C protected the animals against ulcerative intestinal tuberculosis. Smith makes the statement that "the claim that pyorrhea can be prevented or even cured by massive doses of vitamin C has partial justification in the fact that increased capillary resistance in the gums will help to prevent their invasion by pyogenic organisms."

J. F. Rinehart and S. R. Mettier (Am. J. Path. 10: 61 (Jan.) 1934; J. Exper. Med. 59: 97 (Jan.) 1934) suggest that latent scurvy prepares the soil or provides the susceptible hosts in whom, with the added insult of acute infection, develop the characteristic train of symptoms and pathological evolution of acute rheumatic fever. Smith found that when subacute scurvy and infection were combined in the guinea-pigs, lesions strikingly similar to those of rheumatic fever were produced. She says, "should this interrelationship be verified for man, rheumatic fever might be placed in the class of food deficiency diseases, early stages of which might be detectable by the capillary resistance test and checked by increased provision of vitamin C."

*Vitamin D, Calcium and Phosphorus*—A. F. Hess and J. M. Lewis (J. A. M. A. 101: 181 (July 15) 1933) state that irradiated milk seems to be the most desirable antirachitic for prevention on a commercial scale. Only 20 to 24 ounces of milk is needed daily to secure protection. The fact that the ratio of calcium to phosphorus in milk is so satisfactory is probably the reason why vitamin D milk is so beneficial to rachitic infants.

The production of vitamin D milk seems to be under proper control, as is shown by the regulations of the Wisconsin Foundation, April, 1932. They began at that time to issue licenses for the production of vitamin D milk having a potency of not less than 160 Steenbock units per quart. A fee of one dollar per cow per year is charged and the license issued subject to definite feeding instructions. It is necessary to keep a record of the milk production and the amount of yeast fed to the vitamin D herd and a monthly report must be submitted. These items must check with the sales and shipping records of the company that produces the irradiated yeast. A bioassay is made of the milk of each new licensee.

to make certain that it has been properly standardized and occasional bioassays are made thereafter without the knowledge of the producers. In November, 1934, there were 200 high grade dairy farms distributing vitamin D milk.

Direct irradiation is another method used. B. Kramer and I. F. Gittleman (New England J. Med 209 906 (Nov 2) 1933) concluded that at the levels fed there was no significant difference in effectiveness between vitamin D milk prepared by direct irradiation and vitamin D milk produced naturally by feeding cows irradiated yeast. Vitamin D milk is recommended for prevention and correction of dental decay in children and adults. A generous supply should be taken during pregnancy and lactation. In this way an abundance of minerals and vitamin D are provided and permits a prenatal storage of the vitamin by the infant, which usually lessens the possibility of the infant developing rickets after birth.

A few practical reasons are given for using vitamin D milk, *i. e.*, it is simple, it eliminates the bother of giving the children cod-liver oil or viosterol; the children must have milk anyway. Physicians like it because of its uniform vitamin D potency and its proven effectiveness.

**Rôle of Copper**—The function of copper is to mobilize the iron from the reserve stores in the liver and thus act as a sort of catalyzer in the formation of hemoglobin. S. Smith (J. Am. Dietet. A 10.118 (July) 1934) states that it is difficult at present to determine the availability of iron from the different sources for hemoglobin formation, but a method is being checked up for reliability, and should it be satisfactory, it will simplify the present means of determining the potencies of various foods for the prevention and cure of simple nutritional anemia.

Diversified diets may supply sufficient iron and copper for the maintenance of a normal blood stream in adults with normal hemoglobin requirements, but for rapidly growing children and for some adults C. A. Elvehjem (J. Biol. Chem. 103 61 (Nov.) 1933) has found many diets to be low in iron and possibly copper. The value of foods for supplementing diets low in iron and copper must be based upon the amount of available elements, not upon the total content. Diets deficient in blood-forming elements may be rendered complete by the addition of standardized quantities of iron and copper salts.

In pernicious anemia the use of the hog stomach is based upon the theory that there is an intrinsic factor which is present in normal gastric juice which reacts with another extrinsic factor. Wilkinson and Klem explain the relationship between the active anti-anemic substance in stomach and liver thus: Hemopoietin, the stomach active principle (Castle's intrinsic factor) plus unknown constituent of beef or gastric muscle (Castle's extrinsic factor) equals liver active principle.

Because the treatment with hog stomach seems to be superior over oral liver therapy, it is thought that the stomach preparation contains the labile enzyme (intrinsic factor), the substrate (extrinsic factor), and possibly the end point of their reaction (the stable active principle which under normal conditions is stored in the liver).

**Quantitative Aspects of Vitamin Requirements.**—Concerning the quantitative aspects of vitamin requirements, William Salter (J. Am. Dietet. A. 10:296 (Nov.) 1934) concludes that it is no longer considered safe to place too much trust in normal, average figures for vitamin requirements. He says it becomes very important to realize that vitamin requirements may be considerably increased because of pre-existing disease. He mentions the fact that during the last few years watchful physicians have observed the development of vitamin deficiency states on wards of reputable hospitals in patients who were receiving the routine balanced house diet with or without extras. Definite abnormal conditions have increased the vitamin requirements of these individuals, thus causing a vitamin malnutrition. He gives examples. Some cases are associated with intestinal disorders. Parasites may be the cause, as anemia caused by the hookworm. The condition may follow an operation of the bowel, a resection of a considerable part may damage the absorbing surface. C. M. Jones and T. V. Urmy (New England J. Med. 210:251 (Feb. 1) 1934) report a case in which acute intestinal obstruction led to a short circuiting of most of the small intestine. There followed 3 years of limb paralysis and beriberi, due to insufficient vitamin B. The administration of "b-concentrates" in huge doses proved unavailing because the intestinal absorbing surface was inadequate. Only when the surgical short circuit was remedied did the patient recover.

Salter states further that at present it is possible merely to hazard a guess as to the daily vitamin requirements of man. From investigations and experiments he gives the following minimal average values as the daily requirement: 0.3 mg. carotin; 0.5 mg. of vitamin B<sub>1</sub>; 35 mg. of ascorbic acid; and 0.05 mg. of irradiated ergosterol.

**VITAMIN UNITS.**—Hazel E. Munsell (United States Dept. of Agriculture, Bureau of Home Economics, No. 526 (Nov. 22) 1933) enumerates these as follows:

*Vitamin A*—The *Sherman and Munsell unit* for vitamin A, adopted by the present U. S. Pharmacopœia, is that amount of the vitamin which, when fed daily, just suffices to support a rate of gain of 3 grams per week in a standard test animal (rat) during an experimental feeding period of 4 to 8 weeks.

*Vitamin B*—The *Sherman and Chase unit* for vitamin B is that amount of the vitamin which when fed daily will induce a gain of 3 grams per week in a standard test animal during a test period of 4 to 8 weeks.

*Vitamin C*—The *Sherman unit* for vitamin C is that amount of the vitamin which when fed daily will protect a 300-gram guinea-pig during a period of 90 days.

*Vitamin D.*—(a) The *vitamin D unit of the American Drug Manufacturers Association* (A. D. M. A.) is the minimum average daily amount (in mg.) of codliver oil required to produce, in 60 per cent of the animals in any one group, a degree of recalcification represented by a narrow continuous "line" across the metaphysis of the leg bones of the rats which have been kept and fed under the conditions specified in the assay.

The vitamin D content per Gm. of codliver oil is computed by dividing 1000 mg. (1 Gm.) by the determined minimum average daily amount of oil in mg. required to induce the requisite degree of recovery. The average daily dose is understood to be the total amount of codliver oil given divided by the length of the test period, 10 days.

A standard codliver oil to be used as a standard of reference is one that assays 100 A. D. M. A. units per gram.

(b) *The Steenbock vitamin D unit* is the total amount of vitamin D which will produce a narrow line of calcium deposit in the rachitic metaphyses of the distal ends of the radius and ulnæ of standard rachitic rats, in a period of 10 days. This is the unit accepted for "New and Non-official Remedies" by the American Medical Association. Steenbock states that this unit is approximately equivalent to 27 international units.

A "potent" codliver oil assays approximately 13.3 Steenbock units per gram.

The Steenbock unit is 10 times as large as the A. D. M. A. unit or one Steenbock unit is equivalent to 10 A. D. M. A. units.

(c) *Oslo units* (described by Poulsson, University of Oslo). In this method for vitamin D determination the same experimental animal serves both as a control and a test animal. Young rats are placed at 24 days of age on a rachitogenic diet. After 25 days a skiagram is taken of the left knee joint. The test food is then given in daily doses for 6 days. At the end of this time, a second skiagram is made. The activity of the substance tested is judged by comparing the photographs taken at the beginning and the end of the test period. The efficacy of the substance tested is indicated in units per gram on a principle analogous for vitamin A in the U. S. P. From Poulsson's article, however, it is not clear whether the unit value is that amount which produces complete recovery or a certain well-defined partial recovery. He simply states that it is easy to decide whether a substance tested is or is not potent and that the quantitative evaluation of a recovery involves a certain subjective element, but that with practice this can be done with satisfactory regularity.

Bills states that a product assaying 4000 Steenbock units (300D) contains 12,000 Oslo units.

*Vitamin G*—*The Sherman and Bourquin unit* for vitamin G is that amount of the vitamin which will give an average gain of 3 grams per week during 8 weeks in addition to any appreciable gain in a group of standard test animals maintained on the vitamin G free ration.

PROVISIONAL INTERNATIONAL VITAMIN UNITS.—An understanding of vitamin units is complicated at the present time by the fact that the Health Organization of the League of Nations, through its Permanent Commission on Biological Standards, has recently proposed provisional standards and units for vitamins A, B<sub>1</sub>, C, and D. The Commission includes scientists from England, the Continent, and the United States. In the Report of this Permanent Commission issued in Geneva by the League of Nations in 1930 as publication C. H. 1056, the following provisional units are recommended for adoption over specified trial periods varying from 2 to 5 years.

*Vitamin A*—The vitamin A activity of 0.001 mg. (X) of an international standard preparation of carotin (A selected sample of codliver oil to be held in view as a possible secondary standard).

*Vitamin B*—The antineuritic activity of 10 mg. of an international absorption product of rice polishings prepared by the Seidell method.

*Vitamin C*—The vitamin C activity of 0.1 c.c. of fresh lemon juice.

*Vitamin D*—The vitamin D activity of 1 mg. of the international standard solution of irradiated ergosterol.

The report further designates the methods by which the international standards shall be prepared, and the institutions to which their preparation shall be entrusted.

VITAMIN POTENCIES OF COD-LIVER OILS AND OTHER PRODUCTS.—The U. S. Pharmacopœia is now in process of revision and, in harmony with the recommendations on vitamin units of the Permanent Commission on Biological Standardization, it tentatively proposes the following methods of assaying cod-liver oil.

*Vitamin A*.—Assays of codliver oil for vitamin A content shall be made by comparison with the Reference Codliver Oil prepared and distributed by the Food and Drug Administra-

tion of the U. S. Department of Agriculture, the vitamin A potency of which shall have been determined by a method described. This reference codliver oil shall contain a known number of vitamin A units, each unit to be equivalent in growth promoting and relative anti-erophthalmic activity to 1 microgram ( $\mu$ ) or 0.001 mg. of the International Standard carotene.

*Vitamin D.*—Codliver oil shall be assayed for vitamin D content by comparison with a Reference Solution of Irradiated Ergosterol or of codliver oil, prepared and distributed by the Food and Drug Administration of the U. S. Department of Agriculture, which shall contain a known number of vitamin D units, each unit corresponding to the vitamin D activity of 1 mg of the Standard Solution of Irradiated Ergosterol.

At the present time the vitamin A potency of commercial products such as cod-liver oil and haliver oil (halibut liver oil) is given in U. S. Pharmacopœial (Sherman-Munsell) units, while vitamin D potency is measured by A. D. M. A. units, Steenbock units or Oslo units

The Council on Pharmacy and Chemistry of the American Medical Association specified that "an acceptable cod-liver oil is one which has a potency of 400 vitamin A units per gram when tested by the (present) U. S. Pharmacopœial methods" However, the vitamin A values may vary widely. Several manufacturers of cod-liver oil standardize their products to contain 500 vitamin A units per gram, and one claims that his products contain 1000 A units Standardized cod-liver oil contains about 100 A. D. M. A vitamin D units One manufacturer claims that his product contains 150 A. D. M. A. units per gram

The Council on Pharmacy and Chemistry of the American Medical Association has adopted the qualifying phrases 250D, 10D, etc., to designate the vitamin D potency of various preparations as multiples of the vitamin D potency of cod-liver oil of definite potency (containing 13.3 Steenbock units per gram) Thus, viosterol in oil 250D would have a vitamin D potency 250 times that of cod-liver oil or would contain 3333 units (Steenbock) per gram

*Foods Rich in Vitamins A, B, C, D, E, and G.*—In a hearing on this subject, Hazel E. Munsell (United States Dept of Agriculture, Bureau of Home Economics, No 434-R (Feb 1) 1934) states that vitamins are important substances that are essential for good health, growth, vigor, and general well-being of the body They are often described as necessary body regulators, since their function is to stimulate growth and protect health rather than to furnish the material for building tissue or supplying energy Like many other important things in life, vitamins are most appreciated when they are absent As long as vitamins are present in the diet in sufficient quantities, all is well, but as soon as they are lacking or present in insufficient quantities, the disease or abnormal condition that they prevent develops. This explains the names first given specific vitamins, for instance, the "antiscorbutic" or scurvy-preventing vitamin, and the "antirachitic" or rickets-preventing vitamin

The 6 vitamins so far discovered are described below, and a list of foods which are good sources of each is given These foods have been selected on the basis of experimental work done in many laboratories, including the Nutrition Laboratory of the Bureau of Home Economics Further experiments may make it possible to extend the lists to include other foods

*Vitamin A.*—Vitamin A stimulates growth and is necessary for well-being at all ages. Without a regular supply of vitamin A a person loses vitality and may develop infections in the eyes, sinuses, ears, glands of the mouth and throat, and in some instances in the kidneys and bladder. Foods having a yellow or green color are generally rich sources of this vitamin. Green leaves, yellow corn, and sweet potatoes, for instance are better sources than bleached leaves, white corn, and white potatoes. Thin green leaves are very valuable for their vitamin A content.

Vitamin A is called the "fat-soluble vitamin" because it is soluble in fats. It is only slightly soluble in water and is less affected by heat than some of the other vitamins.

#### GOOD SOURCES OF VITAMIN A

##### *Animal Products.*

Codliver oil	Butter.	Milk.	Salmon
Liver	Cream.	Egg yolk	Cheese, whole milk
			Kidney

##### *Plant Products.*

##### *Green and yellow vegetables*

###### *Leafy*

Spinach	Kale	Endive	Beet leaves
Escarole.	Watercress	Chard.	Mustard greens.
Romaine	Turnip tops	Collards	Dandelion greens.
Lettuce, green	Broccoli		Brussels sprouts

###### *Other*

Beans, string, green	Sweet potatoes	Asparagus.
Carrots	Peas	Tomatoes, red and yellow
Celery, green	Squash, yellow	Corn meal, yellow
	Peppers	

###### *Fruits*

Bananas	Muskmelon	Papaya
Apricots	Cherries.	Avocado
Peaches, yellow	Olives, green and ripe	Prunes.
		Pineapple

*Vitamin B.*—This vitamin is necessary for good appetite and also for normal muscle tone in the digestive tract. Loss of appetite and general listlessness, sluggish digestive systems, and nervous irritability result from a continued diet short in vitamin B, while an absolute lack of this vitamin brings on a muscular paralysis or the disease known as beriberi. Vitamin B is very important to the nursing mother and the baby. Without enough of it, the mother's milk may be poor in quality, and with still less of the vitamin, the mother may even fail to secrete milk. Plenty of vitamin B in the mother's diet also helps to provide the infant with vitamin B.

The list of foods containing vitamin B is long, since a large number of foods contain a little. Whole seeds, such as whole grain cereals and nuts are valuable sources because vitamin B is concentrated in the germ portion. Many fruits and vegetables are also good sources.

Vitamin B is destroyed by heat more readily than vitamin A and long cooking of vegetables is therefore undesirable. Also, since this vitamin is very

soluble in water, it may be easily "washed out" in cooking when much water is used. An alkaline substance, like soda, greatly increases the amount of vitamin B destroyed. This is one reason why cooking green vegetables with soda to preserve the green color is very bad practice.

## GOOD SOURCES OF VITAMIN B.

*Animal Products.*

Liver.	Heart	Lean pork.	Oysters.
Kidney.	Egg yolk	Brains.	Milk.

*Plant Products.**Vegetables:*

Asparagus.	Romaine.	Potatoes, white.	Kohlrabi
Spinach.	Turnip greens.	Cabbage.	Okra.
Tomatoes.	Mustard greens.	Collards.	Onions.
Peas.	Chard	Beet leaves.	Parsnips
Kale	Celery	Cauliflower.	Rutabagas.
Snap beans	Sweet potatoes.	Lettuce.	Peppers, green
Dasheens	Carrots.	Broccoli	Turnips.

*Fruits:*

Grapefruit	Pineapple, fresh and canned.	Peaches	Prunes, fresh.
Lemons	Apples	Avocado.	Dates.
Oranges	Watermelon	Grapes.	Cherries
Bananas.		Cantaloupes	Pears

*Seeds:*

Whole Grains—Wheat, rye, corn, rice, barley, oats  
 Nuts—Almonds, walnuts, chestnuts, Brazil nuts, pecans, peanuts  
 Legumes, beans of all kinds, cowpeas, lentils, dried peas.

*Vitamin C.*—A daily supply of vitamin C is essential for children and adults. The necessity of having adequate amounts of vitamin C in the diet is stressed by all who recognize the importance of good "tooth nutrition." Bleeding gums, loose teeth, sore joints, loss of appetite with loss of weight and fatigue, are symptoms that develop when this diet is extremely low or lacking in vitamin C. An acute condition of this kind has long been known as scurvy. Though rare in this country, many borderline cases of scurvy, with such symptoms as sore gums, loose and decayed teeth, and "rheumatism" occur when the diet contains some vitamin C but not sufficient in quantity.

Vitamin C is easily destroyed by heat at fairly low temperatures and is most easily destroyed in an alkaline solution, such as water containing soda. With the exception of tomatoes, cooked foods cannot be depended upon entirely for vitamin C, nor does the body store a supply of this vitamin, hence the need for some raw fruits and raw vegetables every day.

## GOOD SOURCES OF VITAMIN C

*Fruits*

Oranges	Cranberries.	Raspberries
Lemons.	Bananas	Watermelon
Grapefruit.	Peaches, fresh and canned	Muskmelon
Tangerines.	Pineapple, fresh and canned	Currants, black and red
Strawberries.	Cherries.	Gooseberries
		Apples.

GOOD SOURCES OF VITAMIN C (*Continued*).*Vegetables.*

Cabbage.	Brussels sprouts.	Turnip greens
Tomatoes, fresh and canned.	Celery.	Legumes, sprouted
Spinach, fresh and canned.	Parsley.	Rhubarb.
Peas, fresh and canned	Endive.	Cucumbers.
Broccoli.	Peppers.	Cauliflower.
Rutabagas.	Watercress	Radishes.
Collards	Turnips, fresh and canned.	
Snap beans.	Turnip.	

*Vitamin D* —The mineral elements, calcium and phosphorus, are required in the building of teeth and bones, but unless vitamin D is also provided, these tissues will not develop normally, and stunted growth and rickets may result. There are only a few foods that contain vitamin D in large enough quantities to be considered good sources. The chemical substance ergosterol, is changed into vitamin D by ultraviolet light. Foods containing this substance are often exposed to the rays of an ultraviolet lamp and thus enriched with vitamin D. The addition of irradiated ergosterol offers another means of supplying vitamin D to a food product. Human skin also contains a small quantity of ergosterol which may be changed into vitamin D by ultraviolet light. This explains how rickets may be prevented and cured by exposure of the skin to sunlight containing ultraviolet rays.

This vitamin is not easily destroyed by heat, so that ordinary cooking does not affect it.

## GOOD SOURCES OF VITAMIN D

*Excellent sources*

Codliver oil, halibut liver oil and other fish oils

*Other foods that contain some vitamin D*

Egg yolk	Oysters	Butter
Salmon	Sardines	Milk

Foods are enriched with vitamin D by the Steenbock process of irradiation with ultraviolet light.

*Vitamin E* —Vitamin E is essential for reproduction and is known as the antisterility vitamin. It occurs in a great many foods in small quantities but the germ of the wheat grain is an especially rich source. Vegetable oils, green lettuce, and a number of other vegetables contain considerable quantities of vitamin E. It is not readily destroyed by heat.

*Vitamin G* —Vitamin G is essential for well-being at all ages. A continued deficiency of vitamin G causes slowing up of growth or loss of weight, premature appearance of old age, sore mouth, digestive disturbances, and, in time, a sensitiveness and inflammation of the skin. These symptoms are very similar to those of pellagra, a disease common in certain sections of the South where families are known to live on an inadequate diet. Foods that contain vitamin G are beneficial in preventing and curing pellagra. This vitamin occurs in many foods in moderate or small quantities. The best sources are now known as yeast, glandular organs; lean meat; eggs; milk, either whole or skimmed, fresh, canned or dried; green leaves, and the germ portion of cereals.



Like vitamin B, vitamin G is very soluble in water. It withstands the heat of cooking much better than vitamin B, but is destroyed when soda or other alkaline substances are present

### GOOD SOURCES OF VITAMIN G.

#### *Animal Products.*

Whole milk, fresh.	Eggs
evaporated	Meat—liver (beef and pork).
dried.	Kidney.
Skim milk, fresh.	Spleen.
dried.	Heart (beef).
Buttermilk.	Lean cuts of beef, veal, pork or lamb.
Cheese.	Salmon.

#### *Plant Products.*

Green leaves			
Mustard.	Beet tops.	Spinach.	Broccoli.
Kale	Carrot tops.	Watercress.	Cabbage.
Turnip tops.	Collards.	Lettuce.	
Wheat germ			
Yeast.			

**DIETOTHERAPY.—OBESITY DIETS.**—The caloric value of adipose tissue, as determined in a series of obese cases by the removal and analysis of tissue obtained during laparotomy is discussed by A. E. Koehler (California and West Med 41 253 (Oct.) 1934) The average of the analysis was as follows fat, 90 per cent.; protein, 10 per cent; carbohydrate, a trace, means the caloric value of 1 kilogram, 8100 calories (1 pound = 3670 calories) a day, and remaining in nitrogen balance, would consume 1835 calories for the combustion of this fat, and if the caloric intake was 1000 calories, then the total (1000 plus 1850 or 2850 calories) would represent the maintenance caloric value

In examining 36 cases of obese patients, it was found that the majority required a normal number of calories for maintenance, although some were in the vicinity of 1000 and others over 3000 calories

The maintenance requirement decreased gradually on a reducing diet, and the daily weight gradually diminished With a protein intake of about 90 grams and a caloric value of 800 to 1000, the majority (58 per cent) of the cases showed a negative nitrogen balance The protein intake should be 90 to 100 grams and higher in some cases

There was no reason to believe that hydration is an appreciable factor in the majority of cases in decreasing weight loss, as judged by objective findings and studies on blood plasma hydration when periods of observation were extended 3 to 6 months

Undoubtedly the most talked of and most popular obesity diet was the banana and skimmed milk diet, as introduced by G. A. Harrop (J. A. M. A 102 2003 (June 16) 1934) When used as a continuous diet, 1 or 2 large ripe bananas may be used with 1 glass or 250 c.c. of skim milk for both breakfast and lunch The evening meals are restricted to thin soup, a slice of lean meat, fish or fowl, 2 or 3 portions of a 5 per cent vegetable, a slice of bread and butter, and a portion of uncooked fruit Such a diet will contain 1000 to 1200 calories.

The second method involves using bananas and skim milk alone for a period of 10 to 14 days. The strict diet consists of 6 large bananas and 1000 c c of skim milk divided into 3 or more meals

The advantages of this dietary régime are:

1. The banana is a filling food with a negligible fat content. Milk alone becomes monotonous and flat
2. Skim milk has one-half the caloric value of whole milk.
3. This diet followed for 10 to 14 days will bring about a reduction of 4 to 9 pounds in an active person.
4. Fluids without food value, as plain tea or coffee, are permitted freely
5. Six glasses of water besides milk are allowed. Salt is restricted.
6. The diet is simple, readily available, and palatable.

**ARTHRITIC DIET.**—Some new metabolic and nutritional aspects of chronic arthritis have been presented by Ralph Pemberton (*Am J. Digest Dis and Nutrition* 1: 438 (Sept ) 1934), who for many years stressed the importance of a restricted but balanced dietary for arthritis with the curtailment of that fraction which affords most of the calories in the original American diet, *viz.*, the carbohydrates. A low carbohydrate diet, however, while valuable in a restricted sense to all arthritides, can have intensive application only to those cases which have been found upon study to be suitable for it. A diet low in carbohydrate and relatively high in protein has as a necessary physiological consequence, a depletion of the water reserves of the body and under this influence the edema will be observed to disappear.

The writer states that for every dram of carbohydrate stored, 3.6 grams of water are retained; an obvious therapeutic corollary to this is the avoidance of such storage and of such water retention. The subsidence of swelling to be observed under these conditions is accompanied by a constant loss of weight and the establishment of a negative water balance, and usually by clear cut diminution of pain. By the same token, a diet high in protein, or even a condition of starvation in which the individual draws upon his fixed tissues, requires available water for the elimination of either exogenous or endogenous protein metabolites.

**Ill-effects of Certain Foods in the Diet.**—A comparison of the substitute for mother's milk with those of mother's milk was made by (1) Baumlér (*Monatsschr f Kinderh* 60: 336 (Aug 3) 1934). He found that the so-called fruit-milk is nearly equivalent to human milk as regards the nutritive substances, the calories and minerals. It differs from human milk mainly, however, in one factor, *viz.*, its calcium deficiency. Whether feeding the fruit-milk results in the normal development of the nurslings; (2) whether it can replace mother's milk in nurslings with nutritional disturbances, and (3) whether it will prevent rickets and tetany. One case history reveals that a nursing, who since the end of the second month of life had been fed with fruit-milk, had a mild form of *rickets* and also manifested symptoms of *tetany* at the end of the fifth month. This indicates that the fruit-milk does not prevent rickets and tetany, and thus does not have the biologic value of human milk.

**LAXATIVE DIET.**—An experiment for the purpose of determining the laxative effect of a regenerated cellulose in the diet and its influence on mineral balance, was performed on 8 subjects and reported by H. Morgan (J. A. M. A. 102:995 (Mar. 31) 1934). For a control period of 8 days an adequate diet was given, with preliminary and collection periods. The same diet with 20 grams a day of (nitrogen-free, phosphorus-free, and calcium-free) cellulose was given for the following 9-day-test period, with preliminary and collection periods.

The following summary and conclusions were drawn:

1. Twenty grams of regenerated cellulose a day is definitely laxative, as evidenced by (a) an increased weight of evacuated fecal material; (b) an increased number of defecations during the test period; (c) an increased number of defecations during the test period.

2. A tendency toward an increased excretion of nitrogen and a definite increase in the excretion of phosphorus, calcium, and fecal total ash is caused by cellulose ingestion.

3. It is questionable whether the laxative potency of cellulose counterbalances its detrimental effect on mineral retention. The wisdom of giving a high roughage diet to children and patients under marginal mineral intake is severely questioned.

4. The possible injurious effects caused by eating cellulose products over a long period of time are predicated on a very slight basis as the data afford.

**KETOGENIC DIET.**—L. Montagnini (Minerva Med. 1:877 (June 23) 1934) employed the ketogenic diet in the treatment of *asthmatic patients*. The diet consisted chiefly of broth, meat, eggs, egg whites and some green vegetables (spinach). Some of the patients were in grave asthmatic conditions lasting for days, while others had frequent violent attacks. No other forms of hypersensitivity were found in these patients. The patients were normal and well nourished. Daily quantitative determination of acetone and beta-oxybutyric acid was made on the 24-hour specimens of urine. The alkali reserve and the leukocytic formula were determined before and after the diet, during which time no other treatments were given. The patients showed no ill effects from the diet. Montagnini does not believe that there is a primary tendency to alkalosis in bronchial asthma due to the constitution of the asthmatic patient which brings on the attacks; he maintains, however, that the acidifying method depresses the vagal tonus and stimulates the sympathetic and, as such, is a favorable element in the treatment of bronchial asthma. The writer believes that the acidifying diet is essentially a palliative treatment, although the crises disappeared.

There was a general improvement in each case, as the state of artificially produced equilibrium lacked stability and must be continually stimulated. The degree of eosinophilia during the diet was completely independent of the alkaline reserve variation, since the elevated acidotic condition did not bring on the disappearance of the eosinophils, and they were not increased by the alkalotic conditions.

John W. Rector and Warren E. Wheeler (New England J. M. 211:143 (July 26) 1934) treated 14 cases of *chronic urinary tract infection* with ketogenic diets. Practically all the patients had received more or less intensive

therapy previously, with little or only temporary benefit. The diet was used in cases that were essentially afebrile. The average duration of the diet was 15 days. The urine became sterile in 8 of the 14 cases during the course of dietary treatment and remained sterile for 6 months. In 2 cases a satisfactory ketosis could not be produced and sterilization was never effected. They showed demonstrable anatomic deformities of the urinary tract. In 2 other cases the urine was sterile on discharge from the hospital, but infection recurred later. These 2 children resumed a normal diet as soon as the culture became negative. In no case in which the patient remained on the diet for a week or longer after the culture became negative has there been a recurrence. In one case satisfactory ketosis was not attained in the hospital. Later, by using a higher ratio and by restricting the fluids at home, the urine became sterile, but the infection recurred 4 months later.

**Effect of High Fat Diets on Respiratory Metabolism.**—This subject was studied by E. E. Hawley, C. W. Johnson, and J. R. Murlin (J. Nutrition 6:523 (Nov.) 1933). Many respiratory quotients below the theoretical level for oxidation of fat were shown following meals containing varying amounts of butter fat. The occurrence of these low quotients does not depend on the amount of fat taken in the experimental meal, or on the fatty acid-to-dextrose ratio of the general diet, so much as on the tolerance of the subject. Adaptation to or tolerance of high fat in the sense of better capacity to oxidize fat and produce less ketosis, may be acquired and retained for several months. The level of the respiratory quotient bears no intimate relationship to the demonstrable ketosis or ketonuria. Production of glycogen from the protein metabolism could account for a depression of the respiratory quotient at most of 0.025; while production of glycogen from glycerin, assuming that only the glycerin of the fat metabolism was available, would produce a depression of not more than 0.003. Correction of the quotient for the demonstrable ketosis and consequent ammonia formation would not account for more than 0.005. At most, the combined effect of all these factors would not account for quotients lower than 0.69. The formation of glycogen from fat (beyond the amount that could arise from glycerin) having never been proved, it would be premature to conclude that the quotients below 0.69 in this work demonstrated gluconeogenesis from fatty acids. Hawley and her associates suggest, as an alternative explanation, that in the oxidation of fatty acid chains the uptake of oxygen may outrun considerably, for a time, the production of carbon dioxide and thus account for a depression of the respiratory quotient. A process of desaturation that would remove hydrogen but not produce any carbon dioxide, followed by oxidation with production of carbon dioxide, would fulfill the requirements.

**PSORIASIS DIET.**—O. Grütz (Deutsche med. Wchnschr. 60:1039 (July 13) 1934) believes that psoriasis is caused by a disturbance in fat metabolism and that it can be counteracted by a diet deficient in fat. The fats to avoid are bacon, lard, butter, cream, oil, meats with a high fat content such as pork, mutton, goose, duck, certain fish, of which eel, herring, salmon, carp and roe are examples, and egg yolks, because of their high cholesterol content. Cakes and other baked foods containing fats are not permitted. The foods allowed on this

low diet are lean meats, fish with a low fat content, soups and vegetables, prepared without fat or with fat taken off when cold, fruits and berries, preserves, fruit juices, and various breads made without fat. On this diet obese patients having psoriasis frequently lose weight, while others are able to maintain their bodyweight or even increase it by choosing an adequate number of calories from carbohydrate and protein foods. Grütz suggests that just as the carbohydrate tolerance differs in diabetic patients, there may be a difference in the fat tolerance of psoriatic patients. Using clinical manifestations as a basis, it was found that some patients need a slight reduction in their fat intake, while others require a strict régime. It is advisable to investigate whether the fat synthesis is disturbed in psoriatic patients. Although in some patients the lesions spread in area as they decrease in depth shortly after the onset of treatment, the diet should be continued, for it will finally cause a complete disappearance of the lesions, whether 3 weeks or 2 months are required.

**FOOD ALLERGY.**—A. H. Rowe (Am. J. Digest. Dis. and Nutrition 1:387 (Aug.) 1934) has revised his diets for the elimination of positive foods causing allergy. When symptoms of probable food allergy are not controlled by diets excluding foods to which skin reactions have occurred, or if skin reactions to foods are negative, or impossible to perform, elimination diets may be used. The frequency of the negative skin reaction to foods productive of clinical allergy and the occurrence of positive reactions to foods not causative of allergic symptoms should be borne in mind.

1. Diets 1 and 2 first may be prescribed together or separately, modifying them or substituting similar foods for any in the diets to which skin reactions or known idiosyncrasies exist

2 If sensitization to cereals as a group is suspected, Diet 3 may be used initially

3 Suggested menus for Diets 1 and 2, together, and Diets 1, 2, and 3 separately are detailed later. These menus indicate the ease in preparing meals which meet caloric and metabolic requirements and a modified preparation of specified foods in the elimination diets. A reduction of calories is indicated for children of various ages

4 The selected diet must be taken for at least 10 days or even 2 to 3 weeks, for in many cases reacting bodies to the causative foods disappear very slowly from the shock tissue. If relief does not occur, another elimination diet should be tried

5 Absolute adherence to the prescribed diets is imperative. Not the slightest bit of any food not specified must be taken. Restaurant and hotel food often contains slight amounts of forbidden foods, due at times to poorly cleansed cooking utensils. No commercial breads, cookies, soups, etc., should be used unless every ingredient is known.

6 If body weight decreases, specified sugars, starches and oils must be increased. Prescribed fruits and vegetables assure vitamins A, B, C and G. Adequate protein, when milk is excluded, requires meat or other protein 2 or 3 times a day. If milk is excluded longer than 1 month, the addition of 4 to 6 Gm. (1 to 1½ drams) of **dicalcium phosphate** on retiring will assure mineral balance

Vitamin D must be supplemented by **cod-liver oil, halibut oil, viosterol, sun or quartz light therapy**. Until fish is added, fish oils cannot be used, and viosterol should be allowed only in an oil contained in the "elimination diets."

7. With relief of symptoms longer than former periods of freedom, other foods, 1 to 3 at a time, from the remaining "elimination diets," are tried every 4 to 7 days. Thereafter, other vegetables may be added. In 1 to 3 months milk, egg and wheat may be tried separately at fortnightly intervals. If the patient is allergic to any food, symptoms may occur immediately, or in days or even weeks, according to the patient's tolerance. In such cases the food must again be eliminated.

8. In the undernourished or in children, Diet 4 containing milk may be used first, or milk may be tried, added to the chosen "elimination diet" in 1 or 2 weeks. Sobee, a soya bean product, or Cemac, containing beef and vegetables, are available for infants and children who cannot tolerate denatured cow's or goat's milk.

9. Desensitization by elimination may require weeks, months, or even years. With the above precaution, caloric and metabolic requirements are assured.

10. The diagnosis, control and treatment of inhalant and contact allergies which may accompany food sensitization are most important and not infrequently are necessary for satisfactory control of food allergy.

**Supplemental Elimination Diets.**—When Diets 1, 2 and 3 fail to relieve symptoms, the supplemental diets may be tried, or they may be used initially if sensitizations to many different foods or to nearly all members of one or more groups of foods such as cereals, fruits, vegetables or meats are indicated by history or skin reactions.

In the unsolved cases of possible food allergy all the foods must be suspected and minimal diets be selected as follows

1. A choice of 1 or 2 of the following carbohydrates    Rice, corn, tapioca, sago, sweet or white potatoes

2. A choice of 1 or 2 of the following protein rich foods    Lamb, beef, chicken, soya beans, lima beans, dried peas

3. Choice of 1 or 2 of the following vegetables    Spinach, carrots, beets, artichokes, asparagus, peas, tomatoes

4. A choice of one or two of the following fruits    Lemon, grapefruit, pear, peach, apricot, pineapple

5. Mazola (corn), Wesson (cottonseed), olive or sesame oil; white vinegar if lemon is excluded, salt, cane or beet sugar, glucose

During childhood, desensitization to foods may gradually occur even though they are contained in the diet. Such a result may be more apparent than real, however, since one manifestation such as eczema, urticaria, asthma, or gastrointestinal symptoms may be replaced by another, or the food allergy may remain latent to reassert itself in later life. In childhood and especially in adult life, elimination of the allergenic food is the most effective means for desensitization. This may occur spontaneously in a few weeks after the elimination of such food, or may require months or years. Oral and hypodermic desensitization meets with varying results in different hands.

If sensitization to whole groups of food, such as cereals, meats, or fruits is suspected, such groups may be excluded provided the prescribed diet meets

metabolic and caloric requirements. If allergy to meats is suspected, the legumes may be used to furnish necessary protein if they are not productive of sensitization. Menus can be formulated and these supplemented diets may be developed as already suggested for Diets 1, 2 and 3.

**Desensitization to Foods.**—During childhood, desensitization to foods may gradually occur even though they are contained in the diet. Such a result may be more apparent than real, however, since one manifestation such as eczema, urticaria, asthma, or gastrointestinal symptoms may be replaced by another, or the food allergy may remain latent to reassert itself in later years. In childhood and especially in adult life, elimination of the allergenic food is the most effective means for desensitization. This may occur spontaneously in a few weeks after the elimination of such food, or may require months or years. Oral and hypodermic desensitization meets with varying results in different hands. Freeman has reported success with hypodermic therapy in certain food sensitive patients Urbach has also recommended specific prepeptans for the eradication of food allergies. In America, allergists have yet to affirm the value of his suggestions.

**Elimination Diets.**—Elimination diets as aids in the diagnosis and treatment of food allergies again are described. Certain revisions, new menus and recipes have been detailed. Symptoms of suspected food allergy which are not relieved by "test negative" diets may be studied with this elimination method of diet trial. The diets should be modified by positive skin reactions obtained by routine testing with food allergens and by histories of food disagreements. However, it is justifiable to use "elimination diets" modified only by the history of food idiosyncrasies without skin testing if such tests are absolutely unavailable to the physician or patient. Only with the use of diet trial preferably aided by skin reactions can the true frequency of food allergy throughout life be realized.

#### ELIMINATION DIETS (ROWE).

<i>Diet 1</i>	<i>Diet 2.</i>	<i>Diet 3.</i>	<i>Diet 4.</i>
Rice	Corn.	Tapioca.	Milk.*
Tapioca.	Rye.	White and sweet potato.	
Rice biscuit	Corn pone	Lima bean—potato bread	
Rice bread.	Corn rye muffin.	Soya bean—lima bean bread	
	Rye bread		
	Rye crisp.		
Lettuce	Tomato	Beets	
Spinach	Squash.	Carrots.	
Carrot	Asparagus	Lima beans	
Beet	Peas.	String beans	
Artichoke.	String beans.	Tomatoes	
Lamb	Chicken	Beef	
	Bacon.	Bacon	
Lemon	Pineapple.	Lemon	
Grapefruit.	Peaches	Grapefruit	
Pears	Apricot	Peaches	
	Prunes	Apricot.	

\* Milk should be taken up to 2 or 3 quarts a day Tapioca cooked with milk and milk sugar also may be taken

ELIMINATION DIETS (ROWE) (*Continued*).

<i>Diet 1.</i>	<i>Diet 2.</i>	<i>Diet 3</i>
Cane sugar.	Cane sugar.	Cane sugar
Wesson oil.	Mazola oil.	Olive oil.
Olive oil.	Wesson oil.	Wesson oil.
Salt.	Salt.	Gelatin
Gelatin.	Karo corn syrup.	Salt.
Syrup made of maple sugar or cane sugar flavored with maple- line or maple sugar.		Maple syrup or syrup made with cane sugar flavored with maple
Olives.		
Pear butter.		

## DETAILED FOOD LISTS OF ELIMINATION DIETS (ROWE)

## BREAKFAST

*Diets 1 and 2**Approximate Amounts*

## Beverage

- (a) Grapefruit (fresh) juice or lemonade with sugar, if desired 1 glassful.  
 (b) Pineapple juice

## Cereal

- (a) Boiled brown or polished rice or cooked cornmeal served with apricot, peach or prune juice and sugar  $\frac{1}{2}$  cup rice  
 3 teaspoons juice  
 (b) Rice crispies or corn flakes served with grapefruit juice and sugar or with apricot, peach or prune juice or maple syrup  $\frac{3}{4}$  cup dry flakes  
 (c) Cold rice or corn meal fried in Mazola oil or bacon or chicken fat served with maple syrup or Karo corn syrup

## Meat

- (a) Bacon (moderately crisp) or 3 slices or  
 (b) Lamb chops, lamb or chicken croquettes 1 medium chop  
 (c) Lamb kidney fried with bacon

## Bread

- (a) Corn pone 2 muffins or  
 (b) Corn rice muffin 2 slices toasted  
 (c) Corn rye muffin  
 (d) Rice biscuit  
 (e) Rice bread  
 (f) Rye bread  
 (g) Rye crisp

## Jams or Preserves:

- (a) Peach or prune jam 2 tablespoons  
 (b) Apricot or apricot pineapple jam or preserves  
 (c) Grapefruit and lemon marmalade  
 (d) Pear butter

## Fruit

Sliced or whole grapefruit canned, fresh or stewed  
 peaches, apricot, pears, pineapple or prunes



DETAILED FOOD LISTS OF ELIMINATION DIETS (ROWE) (*Continued*).

## LUNCH AND DINNER.

*Diets 1 and 2.**Approximate Amounts.*

## Salad

- (a) Lettuce with apricot, peach, pear or pineapple with oil dressing or special Mayonnaise. 2 halves or slices or
- (b) Vegetable salad made of tomato, carrots, beets, asparagus, peas, string beans or artichokes with oil dressing or special Mayonnaise  $\frac{1}{2}$  cup mixed vegetables  
1 tablespoon oil or dressing.
- (c) Sliced tomato or lettuce-tomato with oil dressing.
- (d) Lemon gelatin with grated carrots and crushed pineapple.

## Soup

- (a) Lamb broth clear or with rice, carrot, peas, string beans, as desired 1 cup
- (b) Chicken broth clear or with rice, carrot, peas, string beans, as desired
- (c) Split pea soup.

## Meat

- (a) Lamb served as chops, roast, tongue or stew made with lamb, rice, corn, carrots, peas, beets or string beans 2 medium chops or
- (b) Chicken—roasted fried, broiled, stewed. May be rubbed with bacon if desired or stuffed with rice or corn meal 1 broiler or equivalent
- (c) Thicken gravy or sauces with rice flour or corn-starch

## Vegetables.

- Spinach, carrot, squash, asparagus, peas, artichokes, beets, tomatoes 4 tablespoon vegetables

## Bread

Choice of those in breakfast

## Jams or Preserves:

Choice of those in breakfast

## Desserts

- (a) Fruit as suggested for breakfast 4 tablespoon fruit
- (b) Rice fruit pudding 1 cup cake
- (c) Tapioca fruit pudding
- (d) Corn-rice cookie or rice cup cakes

## Beverages

- (a) Grapefruit juice or lemonade with sugar 1 glassful  
Corn dextrose may be used if extra carbohydrates is desired



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